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(54) Amino-benzofuryl-and thienyl-derivatives

Aminobenzofuryl- und -thienylderivate

Dérivés de aminobenzofuryle et -thienyle

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(73) Proprietor: **BAYER AG**
51368 Leverkusen (DE)

(72) Inventors:

- Bräunlich, Gabriele, Dr.
D-42115 Wuppertal (DE)
 - Fischer, Rüdiger, Dr.
D-50933 Köln (DE)
 - Es-Sayed, Mazen, Dr.
D-42115 Wuppertal (DE)
 - Hanko, Rudolf, Dr.
D-40237 Düsseldorf (DE)
 - Tudhope, Stephen, Dr.
Windsor Berkshire SL4 4JH (GB)

- Sturton, Graham, Dr.
Bray Maidenhead SL 62 DW (GB)
 - Abram, Trevor, Dr.
Marlow Buckinghamshire (GB)
 - McDonald-Gibson, Wendy J.,Dr.
Wallingford, Oxford, OX 106 HD (GB)
 - Fitzgerald, Mary F., Dr.
Begbroke Oxford OX 51 RN (GB)

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EP-A- 0 146 243 **EP-A- 0 551 662**
EP-A- 0 623 607

- CHEMICAL ABSTRACTS, vol. 77, no. 23, 4 December 1972 Columbus, Ohio, US; abstract no. 151884g, A.E. BRANDSTROM ET AL. 'Pharmacologically active benzofuran derivatives' page 395; column 2;
 - CHEMICAL ABSTRACTS, vol. 78, no. 25, 25 June 1973 Columbus, Ohio, US; abstract no. 159427b, A.E. BRANDSTROM ET AL. 'Benzofuran derivatives' page 401; column 1;

Remarks:

The file contains technical information submitted after the application was filed and not included in this specification

EP 0 685 475 B1

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Description

The invention relates to amino-benzofuryl- and thiienyl-derivatives, processes for their preparation and their use in medicaments.

5 It is known that the NADPH oxidase of phagocytes is the physiological source to the superoxide radical anion and reactive oxygen species derived therefrom which are important in the defence against pathogens. Uncontrolled formation leads to tissue damage in inflammatory processes. It is additionally known that elevation of phagocyte cyclic AMP leads to inhibition of oxygen radical production and that this cell function is more sensitive than others such as aggregation or enzyme release (cf. Inb. Arch. Allergy Immunol., vol. 97: pp 194-199, 1992).

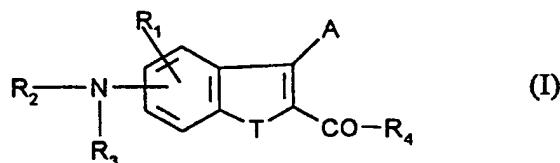
10 Benzofuran- and benzothiophen derivatives having lipoxygenase-inhibiting action are described in the publication EP 146 243.

Surprisingly it was found that compounds given by the general formula (I) inhibited oxygen radical formation and elevated cellular cyclic AMP levels probably by inhibition of phagocyte phosphodiesterase activity.

The invention relates to amino-benzofuryl- and thiienyl-derivatives of the general formula (I)

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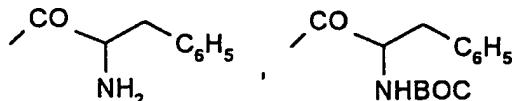
25 in which

I. :

- 30 R^1 represents hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms or represents halogen, carboxyl, cyano, nitro, trifluoromethyl or a group of a formula $-OR^5$, $-SR^6$ or $-NR^7R^8$,
in which
- 35 R^5 , R^6 and R^8 are identical or different and denote hydrogen, cycloalkyl having 3 to 6 carbon atoms, benzyl or a 5 to 7-membered saturated or unsaturated heterocycle having up to 4 heteroatoms from the series comprising N, S and/or O and to which a phenyl ring can be fused and which is optionally substituted by identical or different substituents from the series comprising halogen, cyano, nitro or by a straight-chain or branched alkyl having up to 6 carbon atoms or denote straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, or denote phenyl, which is optionally monosubstituted to disubstituted by identical or different substituents from the series comprising nitro, halogen, carboxy or straight-chain or branched alkoxycarbonyl having up to 6 carbon atoms,
- 40 or
- 45 R^5 denotes a hydroxyl protecting group,
 R^7 denotes hydrogen or a straight-chain or branched alkyl having up to 4 carbon atoms,
 R^2 represents formyl or straight-chain or branched acyl, alkoxy or alkoxycarbonyl each having up to 8 carbon atoms in the alkyl group, or represents benzoyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising halogen, cyano, carboxy, straight-chain or branched alkoxy, alkoxycarbonyl or acyl each having up to 6 carbon atoms in the alkyl group,
or represents a group of a formula

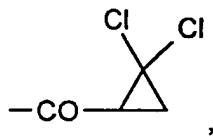
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$-SO_2R^9$, $-CO-(CH_2)_aNR^{10}R^{11}$, $-CO-(CH_2)_bR^{12}$, $-CO-S-R^{13}$ or a residue of the formula

5



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in which

 R^9

denotes straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by phenyl, or denotes phenyl, which is optionally substituted by trifluoromethyl, cyano, nitro or straight-chain or branched alkyl having up to 6 carbon atoms,

15 R^{10} and R^{11}

are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms or phenyl,

 R^{12}

denotes straight-chain or branched hydroxyl, oxyacyl, alkoxy or alkoxy carbonyl each having up to 6 carbon atoms or carboxy,

a

denotes a number 0, 1, 2 or 3,

b

denotes a number 1, 2 or 3,

 R^{13}

denotes straight-chain or branched alkyl having up to 6 carbon atoms,

 R^3

represents hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, or has the abovementioned meaning of R^2 ,

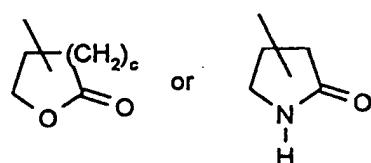
T

represents an oxygen or sulfur atom

25 A

represents hydrogen, hydroxyl, cycloalkyl with 3 to 6 carbon atoms, carboxy or straight-chain or branched alkoxy carbonyl or alkoxy each having up to 6 carbon atoms, or straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms and each of which is optionally monosubstituted by cyano or by a 5 to 7-membered saturated or unsaturated heterocycle having up to 4 heteroatoms from the series comprising N, S and O, which is optionally substituted by identical or different substituents from the series comprising hydroxy, halogen, cyano, nitro or by a straight-chain or branched alkyl having up to 6 carbon atoms, or alkyl or alkenyl are optionally substituted by a group of a formula

35



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in which

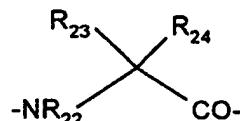
c

denotes a number 1 or 2, and in which both rings are optionally monosubstituted by hydroxy, halogen or by straight-chain or branched alkyl having up to 6 carbon atoms,

45

or alkyl or alkenyl are optionally monosubstituted by a group of a formula -CO-R¹⁴, -CO-NR¹⁵R¹⁶, -CONR¹⁷-SO₂-R¹⁸ or -PO(OR¹⁹)(OR²⁰), -OR²¹ or

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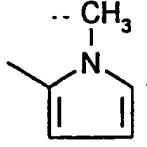


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in which

 R^{14}

denotes hydroxyl, cycloalkyloxy having 3 to 7 carbon atoms or straight-chain or branched alkyl or alkoxy each having up to 8 carbon atoms,

	R^{15} , R^{16} and R^{17}	are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms, phenyl or benzyl, or
5	R^{15} R^{16}	denotes hydrogen, and denotes hydroxyl, or
	R^{15} and R^{16} R^{18}	together with the nitrogen atom form a 5-or 6-membered saturated heterocycle, denotes a straight-chain or branched all having up to 6 carbon atoms, which is optionally substituted by phenyl or trifluoromethyl, or
10		denotes phenyl, which is optionally substituted by substituents from the series comprising halogen, cyano, nitro or by a straight-chain or branched alkyl having up to 6 carbon atoms,
	R^{19} , R^{20} and R^{21}	are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms,
15	R^{22}	denotes hydrogen, an aminoprotecting group or straight-chain or branched alkyl having up to 6 carbon atoms,
	R^{23} and R^{24}	are identical or different and denote hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms, or
20	R^{23}	has the abovementioned meaning, and
	R^{24}	denotes cycloalkyl having 3 to 6 carbon atoms or aryl having 6 to 10 carbon atoms or straight-chain or branched alkyl having up to 8 carbon atoms, which is optionally substituted by cyano, methylthio, hydroxy, mercapto, guanidyl or a group of a formula - $NR^{25}R^{26}$ or $R^{27}-CO-$, wherein
25	R^{25} and R^{26} R^{27}	have the meaning shown above for R^{15} , R^{16} and R^{17} , denotes hydroxyl, benzyloxycarbonyl, straight-chain or branched alkoxy having up to 6 carbon atoms or the abovementioned group - $NR^{25}R^{26}$, or alkyl is optionally substituted by cycloalkyl having 3 to 6 carbon atoms; or by aryl having up to 6 to 10 carbon atoms, which is optionally substituted by hydroxyl, halogen, nitro, straight-chain or branched alkoxy having up to 8 carbon atoms or by the abovementioned group of the formula - $NR^{25}R^{26}$,
30		or alkyl is optionally substituted by indolyl or by a 5 to 6 membered unsaturated heterocycle having up to 4 N-atoms wherein optionally all -NH-functions are protected by straight-chain or branched alkyl having up to 6 carbon atoms or by an amino protecting group, and
35	R^4	represents phenyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, adamantyl, phenoxy, cycloalkyl having up 3 to 6 carbon atoms, halogen, nitro, furanyl, thiienyl, pyridyl, tetrazolyl, trifluoromethyl, difluoromethyl, cyano, carboxyl, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 11 carbon atoms in the alkyl group or by phenyl, which is optionally monosubstituted to trisubstituted by nitro, halogen, formyl, carbonyl or straight chain or branched alkoxy, acyl, alkoxy carbonyl or alkyl each having up to 6 carbon atoms, which is optionally substituted by hydroxyl or phenyl is substituted by a group of formula - $NR^{28}R^{29}$, - SR^{30} , SO_2R^{31} , -O-SO ₂ R ³² or
40		
45		
50		
55	R^{28} and R^{29} R^{28}	in which have the meaning shown above for R^{10} and R^{11} , or denotes hydrogen,

and

- 5 R²⁹ denotes straight-chain or branched acyl having up to 6 carbon atoms,
 R³⁰ denotes straight-chain or branched alkyl having up to 6 carbon atoms,
 R³¹ and R³² are identical or different and represent straight-chain or branched alkyl having up to 6 carbon atoms, benzyl or phenyl, which are optionally substituted by trifluoromethyl, halogen or straight-chain or branched all having up to 6 carbon atoms,

with the proviso that A does not denote methyl
or

10 II. :
if A represents a methyl group

15 R¹, T and R⁴ have the meaning described in part I.

and in this case

20 R² and R³ are identical or diffent and represent hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, or represent formyl or straight-chain or branched acyl, alkoxy or alkoxy carbonyl each having up to 8 carbon atoms,
or represent benzoyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising halogen, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl each having up to 6 carbon atoms,

25 or represent a group of a formula -SO₂(NH)₈R³³, SO₂NH₂, -CO-(CH₂)_dNR³⁴R³⁵, -(CH₂)_e-CO-R³⁶, -CO-(CH₂)_fR³⁷ or -CO-X,
in which

30 R³³ has the abovementioned meaning of R⁹ and is identical or different to the latter,

R³⁴ and R³⁵ are identical or different and have the abovementioned meaning of R¹⁰ and R¹¹,

R³⁶ denotes hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms,

35 R³⁷ has the abovementioned meaning of R¹² or denotes straight-chain or branched alkoxy or oxyacyl each having up to 6 carbon atoms or hydroxyl,

d has the abovementioned meaning of a,

e denotes a number 1, 2, 3, 4 or 5,

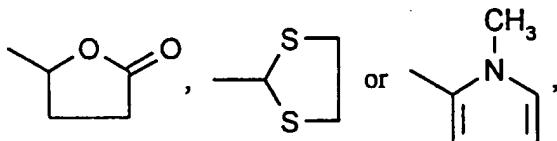
f has the abovementioned meaning of b,

g denotes a number 0 or 1,

X denotes a 5-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the serie comprising N, S and/or O, which is optionally monosubstituted to trisubstituted by nitro, methyl or ethyl,

40 or

X denotes a residue of the formula



50

or

55 III. :

R¹, A and T have the meaning described in part I

or

A represents methyl,
 R² and R³ have the meaning described in part II,

5

and in this case

R⁴ represents a 5 to 7 membered, saturated or unsaturated heterocycle, which can contain up to three oxygen, sulphur and/or nitrogen atoms as heteroatoms and to which further a benzene ring can be fused and wherein both rings are optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, halogen, nitro, 1H-tetrazolyl, trifluoromethyl, trifluoromethoxy, difluoromethyl, difluoromethoxy, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 8 carbon atoms or by a group of formula -NR³⁸R³⁹, -SR⁴⁰, SO₂R⁴¹ or -O-SO₂R⁴²,
 10 in which
 R³⁸ and R³⁹ have the meaning shown above for R²⁸ and R²⁹ and are identical to the latter or different from the latter,
 R⁴⁰ has the abovementioned meaning of R³⁰,
 R⁴¹ and R⁴² are identical or different and have the abovementioned meaning of R³¹ and R³²,
 15 20 and salts thereof.

The amino-benzofuryl- and thienyl-derivatives according to the invention can also be present in the form of their salts. In general, salts with organic or inorganic bases or acids may be mentioned here.

25 Physiologically acceptable salts are preferred in the context of the present invention. Physiologically acceptable salts of the amino-benzofuryl- and thienyl-derivatives can be metal or ammonium salts of the substances according to the invention, which contain a free carboxylic group. Those which are particularly preferred are, for example, sodium, potassium, magnesium or calcium salts, and also ammonium salts which are derived from ammonia, or organic amines, such as, for example, ethylamine, di- or triethylamine, di- or triethanolamine, dicyclohexylamine, dimethylaminoethanol, arginine, lysine or ethylenediamine.

30 Physiologically acceptable salts can also be salts of the compounds according to the invention with inorganic or organic acids. Preferred salts here are those with inorganic acids such as, for example, hydrochloric acid, hydrobromic acid, phosphoric acid or sulphuric acid, or salts with organic carboxylic or sulphonic acids such as, for example, acetic acid, maleic acid, fumaric acid, malic acid, citric acid, tartaric acid, ethanesulphonic acid, benzenesulphonic acid, tol-
 35 uenesulphonic acid or naphthalenedisulphonic acid.

35 The compounds according to the invention can exist in stereoisomeric forms which either behave as image and mirror image (enantiomers), or which do not behave as image and mirror image (diastereomers). The invention relates both to the antipodes and to the racemate forms, as well as the diastereomer mixtures. The racemate forms, like the diastereomers, can be separated into the stereoisomerically uniform constituents in a known manner.

40 Hydroxyl protective group in the context of the above-mentioned definition in general represents a protective group from the series comprising: trimethylsilyl, tert.butyl-dimethylsilyl, benzyl, 4-nitrobenzyl, 4-methoxybenzyl, acetyl, tetrahydropyranyl and benzoyl.

45 Heterocycle in general represents a 5- to 7-membered, preferably 5- to 6-membered, saturated or unsaturated ring which can contain up to four oxygen, sulphur and/or nitrogen atoms as heteroatoms and to which further benzene ring can be fused.

The following are mentioned as preferred: thienyl, furyl, pyrrolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxazolyl, cinnolyl, thiazolyl benzothiaazolyl, isothiazolyl, benzisothiazolyl, oxazolyl, benzoxazolyl, isoxazolyl, imidazolyl, benzimidazolyl, indolyl, morpholinyl, pyrrolidinyl, piperidyl or piperazinyl.

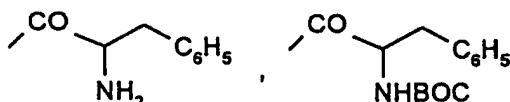
Preferred compounds of the general formula (I) are those
 50 in which

I. :

R¹ represents hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms or represents fluorine, chlorine, bromine, nitro, trifluoromethyl or a group of a formula -OR⁵, -SR⁶ or -NR⁷R⁸,
 55 in which
 R⁷ denotes hydrogen or a straight-chain or branched alkyl having up to 3 carbon atoms,
 R⁵, R⁶ and R⁸ are identical or different and denote hydrogen, cyclopropyl, cyclopentyl, cyclohexyl, chinolyl, pyri-

dyl, imidazolyl, 1,3-thiazolyl or thienyl, which are optionally substituted by identical or different substituents from the series comprising fluorine, chlorine, bromine, iodine, cyano, nitro or by a straight-chain or branched alkyl having up to 5 carbon atoms, or
 5 denote straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms, or
 denote phenyl, which is optionally monosubstituted to disubstituted by identical or different substituents from the series comprising nitro, fluorine, chlorine, bromine, iodine, carboxy or straight-chain or branched alkoxy carbonyl having up to 5 carbon atoms,
 or

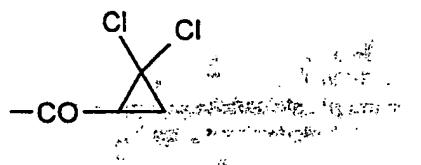
- 10 R⁵ denotes benzyl, acetyl or tetrahydropyranyl,
 R² represents formyl or straight-chain or branched acyl, alkoxy or alkoxy carbonyl each having up to 6 carbon atoms in the alkyl group,
 or represents benzoyl, which is optionally monosubstituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl each having up to 4 carbon atoms in the alkyl group,
 15 or represents a group of a formula



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-SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO-(CH₂)_b-R¹², -CO-S-R¹³ or a residue of the formula

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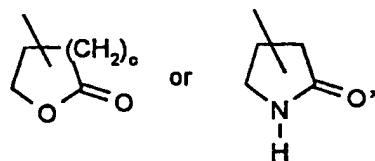


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in which

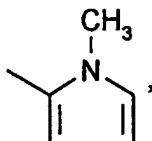
- 35 R⁹ denotes straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally substituted by phenyl, or denotes phenyl, which is optionally substituted by trifluoromethyl, cyano, nitro or straight-chain or branched alkyl having up to 4 carbon atoms,
 R¹⁰ and R¹¹ are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms or phenyl,
 R¹² denotes straight-chain or branched alkoxy carbonyl having up to 4 carbon atoms or carboxy,
 40 a denotes a number 0, 1, 2 or 3,
 b denotes a number 1, 2 or 3,
 R¹³ denotes straight-chain or branched alkyl having up to 4 carbon atoms,
 R³ represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms, or has the abovementioned meaning of R²,
 45 T represents an oxygen atom
 A represents hydrogen, hydroxyl, cyclopropyl, cyclobutyl, cyclopentyl, carboxyl or straight-chain or a branched alkoxy carbonyl or alkoxy each having up to 4 carbon atoms, or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms and each of which is optionally monosubstituted by cyano, tetrazolyl, oxazolyl, oxazolinyl, thiazolyl or a group of a formula

50



55

- in which
- 5 c denotes a number 1 or 2
and in which all rings are optionally monosubstituted by hydroxy, fluorine, bromine, chlorine or by straight-chain or branched alkyl having up to 4 carbon atoms,
or alkyl or alkenyl are optionally monosubstituted by a group of a formula -CO-R¹⁴, -CO-NR¹⁵R¹⁶
or -OR²¹,
- 10 R¹⁴ in which
denotes hydroxyl, cyclopropoxy, cyclopentyloxy, cyclohexyloxy or straight-chain or branched alkyl or alkoxy each having up to 6 carbon atoms,
- 15 R¹⁵ and R¹⁶ are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms, phenyl or benzyl,
or
R¹⁵ denotes hydrogen,
and
R¹⁶ denotes hydroxyl,
or
R¹⁵ and R¹⁶ together with the nitrogen atom form a pyrrolidinyl, morpholinyl or a piperidinyl ring,
R²¹ represents hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms,
and
- 20 R⁴ represents phenyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, adamantyl, phenoxy, cyclopropyl, cyclopentyl, cyclohexyl, fluorine, chlorine, bromine, iodine, nitro, tetrazolyl, furanyl, thienyl, pyridyl, trifluoromethyl, difluoromethyl, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxycarbonyl or acyl each having up to 10 carbon atoms in the alkyl group, or
by phenyl, which is optionally monosubstituted to trisubstituted by fluorine, chlorine, bromine, nitro, formyl or straight-chain or branched alkoxy, acyl, ethoxycarbonyl or alkyl each having up to 4 carbon atoms, which is optionally substituted by hydroxyl, or
phenyl is substituted by a group of formula -NR²⁸R²⁹, -SR³⁰, -SO₂R³¹,
-O-SO₂R³² or
- 25 R²⁸
- 30 R²⁹
- 35 R³⁰



- 40 R²⁸ and R²⁹ in which
have the meaning shown above for R¹⁰ and R¹¹,
or
R²⁸ denotes hydrogen, and
R²⁹ denotes straight-chain or branched acyl having up to 6 carbon atoms,
R³⁰ denotes straight-chain or branched alkyl having up to 4 carbon atoms,
45 R³¹ and R³² are identical or different and represent straight-chain or branched alkyl having up to 5 carbon atoms or phenyl, which is optionally substituted by trifluoromethyl, fluorine, chlorine, bromine or straight-chain or branched alkyl having up to 3 carbon atoms,

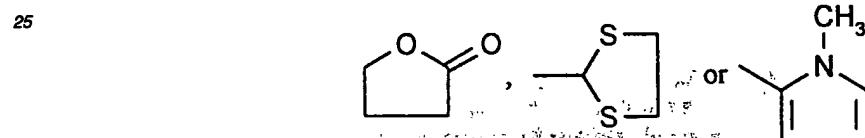
50 with the proviso that A does not denote methyl,
or
II.:
if A represents a methyl group

55 R¹, T and R⁴ have the meaning described in part I,

and in this case

R² and R³ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4

- carbon atoms, or
 represent formyl or straight-chain or branched acyl, or alkoxy carbonyl each having up to 4 carbon atoms,
 5 or represent benzoyl, which is optionally substituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl each having up to 4 carbon atoms,
 or represent a group of a formula $\text{-SO}_2\text{(NH)}_9\text{R}^{33}$, SO_2NH_2 , $\text{-CO-(CH}_2\text{)}_d\text{NR}^{34}\text{R}^{35}$, $\text{-(CH}_2\text{)}_e\text{CO-R}^{36}$, $\text{-CO-(CH}_2\text{)}_f\text{R}^{37}$ or CO-X ,
 in which
- 10 R^{33} has the abovementioned meaning of R^9 and is identical or different to the latter,
 R^{34} and R^{35} are identical or different and denote hydrogen or methyl,
 R^{36} denotes hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms or carboxy,
 R^{37} has the abovementioned meaning of R^{12} or denotes hydroxyl or straight-chain or branched alkoxy or oxacyl each having up to 4 carbon atoms,
- 15 d has the abovementioned meaning of a ,
 e denotes a number 1, 2, 3 or 4,
 f has the abovementioned meaning of c ,
 g denotes a number 0 or 1,
 X denotes pyrrolyl, furyl or isoxazolyl, which are optionally monosubstituted to trisubstituted by nitro, methyl or ethyl
- 20 or
 X denotes a residue of the formula



or

35 III.:

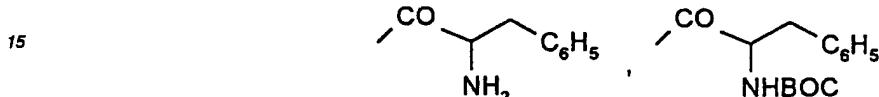
- R^1 , A and T have the meaning described in part I,
 or
- 40 A represents methyl,
 R^2 and R^3 have the abovementioned meaning described in part II
 and in this case
- 45 R^4 represents pyridyl, imidazolyl, pyrazolyl, thieryl, isothiazolyl, 1,3-thiazolyl or benzo[b]thiophenyl, where all rings are optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, fluorine, chlorine, bromine, iodine, nitro, 1H-tetrazolyl, trifluoromethyl, trifluoromethoxy, difluoromethyl, difluoromethoxy, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 6 carbon atoms or by a group of formula $\text{-NR}^{38}\text{R}^{39}$, -SR^{40} , $\text{-SO}_2\text{R}^{41}$ or $\text{-O-SO}_2\text{R}^{42}$,
- 50 in which
 R^{38} and R^{39} have the meaning shown above for R^{28} and R^{29} and are identical to the latter or different from the latter,
 R^{40} has the abovementioned meaning of R^{30} ,
 R^{41} and R^{42} are identical or different and have the abovementioned meaning of R^{31} and R^{32} ,
- 55 and salts thereof.

Particularly preferred compounds of the general formula (I) are those

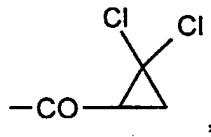
in which

I.:

- 5 R¹ represents hydrogen, straight-chain or branched alkyl having up to 3 carbon atoms, fluorine, chlorine, bromine, nitro or trifluoromethyl,
 R² represents formyl or straight-chain or branched acyl, or alkoxy carbonyl each having up to 5 carbon atoms in the alkyl group,
 or represents benzoyl, which is optionally substituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl, each having up to 3 carbon atoms in the alkyl group,
 10 or represents a group of a formula



- 20 -SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO-(CH₂)_b-R¹², -CO-S-R¹³ or a residue of the formula



- 30 in which
 R⁹ denotes straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally substituted by phenyl, or
 denotes phenyl, which is optionally substituted by trifluoromethyl, cyano or straight-chain or branched alkyl having up to 3 carbon atoms,
 35 R¹⁰ and R¹¹ are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 3 carbon atoms or phenyl,
 R¹² denotes straight-chain or branched alkoxy carbonyl having up to 3 carbon atoms or carboxy,
 a denotes a number 0, 1, 2 or 3,
 b denotes a number 1, 2 or 3,
 40 R¹³ denotes straight-chain or branched alkyl having up to 3 carbon atoms,
 R³ represents hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms, or has the abovementioned meaning of R²,
 T represents an oxygen or sulfur atom,
 A represents hydrogen, hydroxyl, cyclopropyl, cyclobutyl, cyclopentyl, carboxyl, or straight-chain or a branched alkoxy carbonyl or alkoxy each having up to 3 carbon atoms, or straight-chain or branched alkyl having up to 5 carbon atoms which is optionally monosubstituted by cyano or by a group of a formula -CO-R¹⁴, -CO-NR¹⁵R¹⁶,
 in which
 45 R¹⁴ denotes hydroxyl, cyclopropyl oxy, cyclopentyl oxy, cyclohexyl oxy or straight-chain or branched alkyl or alkoxy having up to 5 carbon atoms,
 R¹⁵ and R¹⁶ are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 3 carbon atoms or phenyl,

55 and
 R⁴ represents phenyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, adamantyl, phenoxy, N-methyl-pyrrolyl, cyclopropyl, cyclopentyl, cyclohexyl, fluorine, chlorine, bromine, furanyl, thiienyl, pyridyl, nitro, trifluoromethyl, difluoromethyl, cyano,

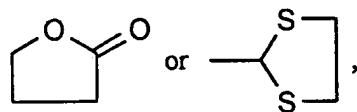
carboxyl, methythio, straight-chain or branched alkyl, alkoxy, acyl or alkoxy carbonyl each having up to 9 carbon atoms, or
 by phenyl, which is optionally monosubstituted to trisubstituted by fluorine, chlorine, bromine, nitro, formyl or straight-chain or branched alkoxy, alkoxy carbonyl, acyl or alkyl each having up to 4 carbon atoms, which is 5
 optionally substituted by hydroxyl,

with the proviso that A does not denote methyl,
 or
 II.:
 10 if A represents a methyl group,

R¹, T and R⁴ have the meaning described in part I.,

and in this case

15 R² and R³ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms, or
 represent formyl or straight-chain or branched acyl or alkoxy carbonyl each having up to 4 carbon atoms,
 20 or represent benzoyl, which is optionally substituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, straight-chain or branched alkoxy or alkoxy carbonyl each having up to 3 carbon atoms,
 or represent a group of a formula -CO-NH₂, SO₂(NH)₉R³⁷, -SO₂NH₂, -(CH₂)₆-CO-R³⁶, -CO-(CH₂)₇R³⁷ or -CO-X,
 25 in which
 R³³ has the abovementioned meaning of R⁹ and is identical or different to the latter,
 R³⁴ and R³⁵ are identical or different and denote hydrogen or methyl,
 R³⁷ has the abovementioned meaning of R¹² or denotes hydroxyl or straight-chain or branched alkoxy or oxacyl each having up to 4 carbon atoms,
 30 R³⁶ denotes hydroxyl or straight-chain or branched alkoxy having up to 3 carbon atoms,
 d has the abovementioned meaning of a,
 e denotes a number 1, 2, 3 or 4,
 f has the abovementioned meaning of b,
 g denotes a number 0 or 1,
 35 X denotes pyrrolyl, N-methyl-pyrrolyl, furyl or isoxacolyl, which are optionally monosubstituted to trisubstituted by nitro, methyl or ethyl,
 or
 40 X denotes a residue of the formula



50 b denotes a number 1 or 2,
 or
 55 III.:

R¹, A and T have the abovementioned meaning described in part I.,

or

- 5 A represents methyl,
in which
R² and R³ have the meaning described in part II,

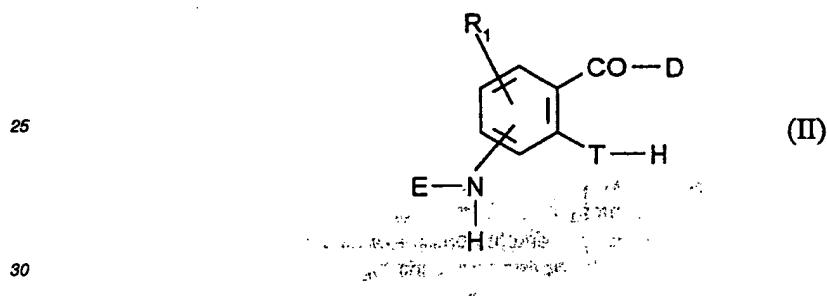
and in this case

- 10 R⁴ represents pyridyl, which optionally is up to substituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, fluorine, chlorine, bromine, nitro, trifluoromethyl, trifluoromethoxy, difluoromethyl, difluoromethoxy, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 5 carbon atoms,

15 and salts thereof.

15 A process for the preparation of the compounds of the general formula (I) has additionally been found, characterized in that

- 20 [A] compounds of the general formula (II)



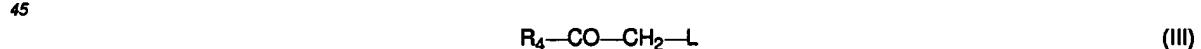
in which

- 35 R¹ and T have the abovementioned meaning,
and

- 40 E denotes straight-chain or branched acyl having up to 4 carbon atoms, preferably acetyl,
and

45 D represents -(CH₂)₂-(C₁-C₄)-alkoxycarbonyl,

by reaction with compounds of the formula (III)

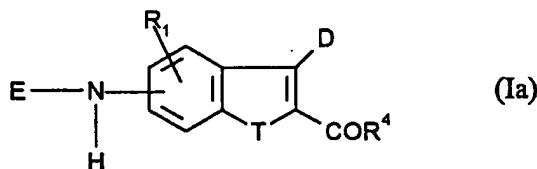


in which

- 50 R⁴ has the abovementioned meaning
and

- 55 L represents a leaving group such as chlorine, bromine, tosylate or mesylate,
in inert solvents in the presence of a base,
firstly are converted into compounds of the general formula (Ia)

5



(Ia)

10

in which

R¹, T, D and E have the abovementioned meaning, and then the compounds (Ia)
are reacted with compounds of the formula (IV) or (IVa)

15

R²-L' (IV)

R³-L' (IVc)

in which

20

R² and R³ have the abovementioned meaning,

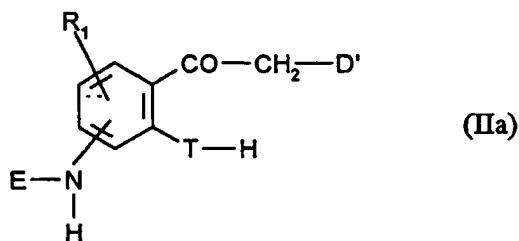
and

25

L' has the abovementioned meaning of L and is identical or different to the latter,

in inert solvents, if appropriate, in the presence of a base,
and in the case of other radicals mentioned for the meaning of substituent A
D is varied, if appropriate, by splitting off protecting groups, alkylation and/or hydrolysis, or
[B] and in the case of A = CH₂-CO-R¹⁴
first compounds of the general formula (IIa)

35



(IIa)

40

in which

45

E, T and R¹ have the abovementioned meaning

and

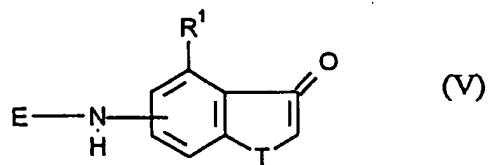
50

D' denotes halogen, preferably chlorine,

are converted in the presence of NaAc and an alcohol, preferably ethanol, to compounds of the general formula (V)

55

5



10

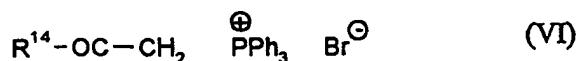
in which

R¹, E and T have the abovementioned meaning,

15

then are reacted with compounds of the general formula (VI)

20

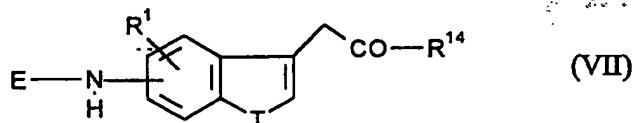


35

in which

R¹⁴ has the abovementioned meaning

to compounds of the general formula (VII)



40

in which

E, R¹, T and R¹⁴ have the abovementioned meaning,

45

in inert solvents,
and in a last step are reacted with compounds of the general formula (VIII)



50

in which

R⁴ and L' has the abovementioned meaning,

in the presence of 'SnCl₄,

and

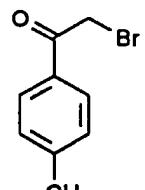
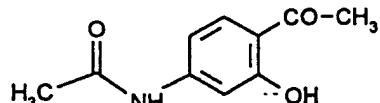
optionally followed by reacting with compounds of the general formulae (IV) or (IVa).

55

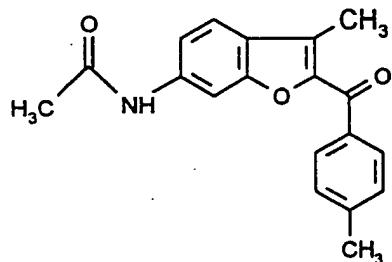
The process according to the invention can be illustrated by way of example by the following equations:

[A]

5

DMF, K₂CO₃

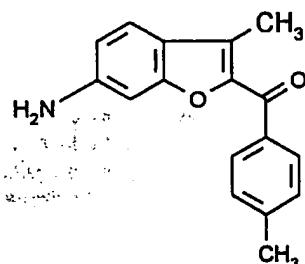
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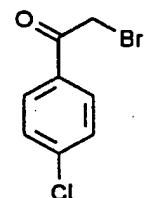
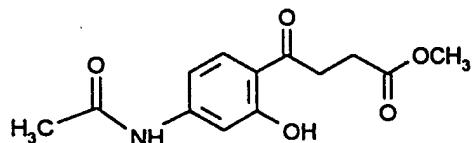
p-toluene/sulfonic acid x HCl

methanol

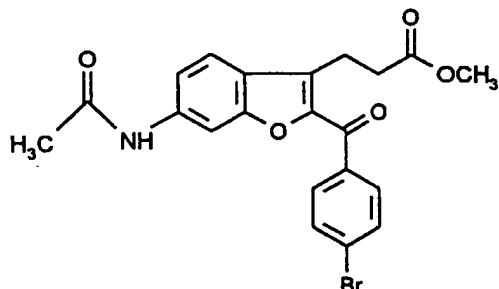
25



35

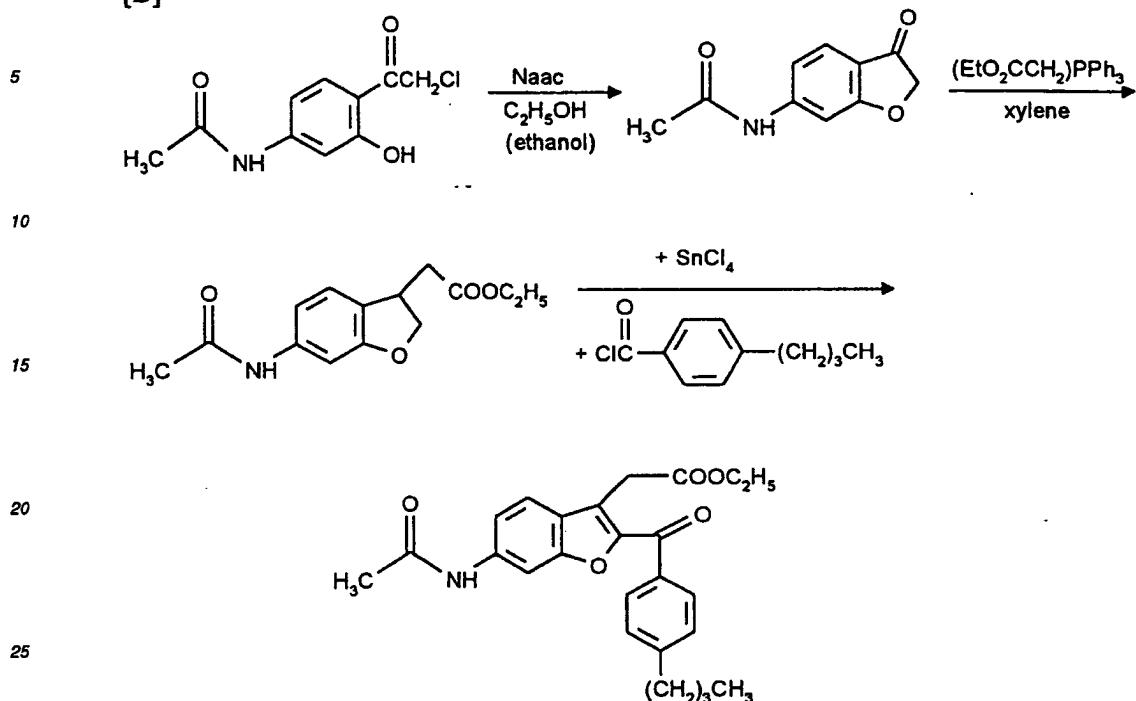
DMF, K₂CO₃

45



55

[B]



30 Suitable solvents are customary organic solvents which do not change under the reaction conditions. These include ethers such as diethyl ether, dioxane or tetrahydrofuran, acetone, dimethylsulfoxide, dimethylformamide or alcohols such as methanol, ethanol, propanol or halogenohydrocarbons such as dichlormethane, trichloromethane, tetrachloromethane or xylol. Methanol, dichloromethane and xylol are preferred.

35 Suitable bases generally are inorganic or organic bases. These preferably include alkali metal hydroxides such as, for example, sodium hydroxide, sodium hydrogencarbonate or potassium hydroxide, alkaline earth metal hydroxides such as, for example, barium hydroxide, alkali metal carbonates such as sodium carbonate, potassium carbonate, alkaline earth metal carbonates such as calcium carbonate, or alkaline metal oder alkaline earth metal alkoxides such as sodium methoxide or potassium methoxide, sodium ethoxide or potassium ethoxide or potassium tert.butoxide, or
40 organic amines (trialkyl(C₁-C₆)amines such as triethylamine, or heterocycles such as 1,4-diazabicyclo[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), or amides such as sodium amides, lithium butyl amide or butyl-lithium, pyridine or methylpiperidine. It is also possible to employ alkali metals, such as sodium or its hydrides such as sodium hydride, as bases. Potassium carbonate, triethylamine sodium hydrogencarbonate and sodium-hydroxide are preferred.

45 The base is employed in an amount from 1 mol to 10 mol, preferably from 1.0 mol to 4 mol, relative to 1 mol of the compounds of the general formula (III).

The compounds of the general formula (Ia) are new and can be prepared as shown above.

The compounds of the general formula (II), (IIa), (III), (IV), (IVa), (V), (VI), (VII) and (VIII) are known or can be prepared by published methods.

50 The compounds according to the invention specifically inhibit the production of superoxide by polymorphonuclear leucocytes (PMN) without impairing other cell functions such as degranulation or aggregation. The inhibition was mediated by the elevation of cellular cAMP probably due to inhibition of the type IV phosphodiesterase responsible for its degradation

They can therefore be employed in medicaments for controlling acute and chronic inflammatory processes.

55 The compounds according to the invention are preferably suitable for the treatment and prevention of acute and chronic inflammations of the airways, such as emphysema, alveolitis, shock lung, asthma, bronchitis, arteriosclerosis, arthrosis, inflammations of the gastrointestinal tract and myocarditis. The compounds according to the invention are additionally suitable for reducing the damage to infarct tissue after reoxygenation. In this case the simultaneous admin-

istration of allopurinol to inhibit xanthine oxidase is of advantage. Combination therapy with superoxide dismutase is also of use.

Test description

5

1. Preparation of human PMN

Blood was taken from healthy subjects by venous puncture and neutrophils were purified by dextran sedimentation and resuspended in the buffered medium.

10

2. Inhibition of FMLP-stimulated production of superoxide radical anions. Neutrophils ($2.5 \times 10^5 \text{ ml}^{-1}$) were mixed with cytochrome C (1.2 mg/ml) in the wells of a microtitre plate. Compounds according to the invention were added in dimethyl sulphoxide (DMSO). Compound concentration ranged from 2.5 nM to 10 μM , the DMSO concentration was 0.1% v/v in all wells. After addition of cytochalasin b (5 $\mu\text{g} \times \text{ml}^{-1}$) the plate was incubated for 5 min at 37°C. Neutrophils were then stimulated by addition of $4 \times 10^{-8} \text{ M}$ FMLP and superoxide generation measured as super-
15 oxide dismutase inhibitable reduction of cytochrome C by monitoring the OD₅₅₀ in a Thermomax microtitre plate spectrophotometer. Initial rates were calculated using a Softmax kinetic calculation programme. Blank wells contained 200 units of superoxide dismutase.

The inhibition of superoxide production was calculated as follows:

20

$$\frac{[1 - ((Rx - Rb))]}{(Ro - Rb)} \cdot 100$$

25

Rx = Rate of the well containing the compound according to the invention.

Ro = Rate in the control well.

30

Rb = Rate in the superoxide dismutase containing blank well.

3. Measurement of PMN cyclic AMP concentration

The compounds according to the invention were incubated with $3.7 \times 10^6 \text{ PMN}$ for 5 min at 37°C before addition of $4 \times 10^{-8} \text{ M}$ FMLP. After 6 min protein was precipitated by the addition of 1% v/v conc. HCl in 96% v/v ethanol containing 0.1 mM EDTA. After centrifugation the ethanolic extracts were evaporated to dryness under N₂ and resuspended in 50 mM Tris/HCl pH 7.4 containing 4 mM EDTA. The cyclic AMP concentration in the extracts was determined using a cyclic AMP binding protein assay supplied by Amersham International plc. Cyclic AMP concentrations were expressed as percentage of vehicle containing control incubations.

4. Assay of PMN phosphodiesterase

40

PMN suspensions (10^7 cells/ml) were sonicated for 6 x 10 sec on ice.

Aliquots (100 μl) were incubated for 5 min at 37°C with the compounds according to the invention or vehicle before the addition of ³H-cAMP (1 mM and 200 nCi per incubation). After 20 min the reaction was stopped by heating at 100°C for 45 seconds. After cooling 100 mg of 5'-nucleotidase was added to each tube and the samples incubated for 15 min at 37°C. The conversion to ³H-adenosine was determined by ion-exchange chromatography on Dowex AG-1x (chloride form) followed by liquid scintillation counting. Percentage inhibition was determined by comparison to vehicle containing controls.

5. Effect of intravenously administered compounds on the FMLP-induced skin oedema guinea pigs

Guinea pigs (600 - 800 g) were anaesthetized with pentobarbitone sodium (40 mg/kg, i.p.) and injected (i.v.) with a 0.5 ml mixture of pentamine sky blue (5% W/V) and ¹²⁵I-HSA (1 $\mu\text{l}/\text{animal}$). 10 minutes later 3 intradermal injections of FMLP (10 $\mu\text{g}/\text{site}$), 1 injection of histamine (1 $\mu\text{g}/\text{site}$) and 1 injection of vehicle (100 μl of 0.2% DMSO V/V in Hanks Buffered salt solution) were made on the left hand side of the animal (preinjection sites). 5 minutes later the drug (1 ml/kg) or the vehicle (50% PEG 400 V/V in distilled water, 1 mg/kg) was administered (i.v.). 10 minutes later an identical pattern of interadermal injections was made on the opposite flank of the animal (post-injection sites). These responses were allowed to develop for 15 minutes before the animal was sacrificed and a blood sample taken.

Skin sites and plasma samples were counted for 1 minute on a gamma counter and the degree of oedema calculated as μl plasma/skin site. Statistical analysis was done by a paired t-test on the mean of the 3 preinjection site values of μl plasma obtained for FMLP/animal. The percentage inhibition of drug or vehicle was calculated as follow

$$X\% = 1 - \frac{\bar{X} \mu\text{l plasma (post-injection site)}}{\bar{X} \mu\text{l plasma (pre-injection site)}} \times 100$$

- 5 6. Effect of orally administered compounds on the FMLP-induced skin oedema of guinea-pigs
in vivo Test's p.o.
Guinea-pigs (600 - 800 g) were fasted overnight and orally treated with vehicle (1% Tylose w/v at 5 ml/kg) or drug (10 mg/kg; 2 mg/ml in 1% Tylose at 5 ml/kg) 40 minutes later the animals were anesthetized with pentobarbitone sodium (40 mg/kg, i.P.) and 0.6 ml of a mixture of pontamine sky blue (5% w/v) and ^{125}I -HSA (1 $\mu\text{ci}/\text{animal}$) was injected (i.v.). 90 minutes after oral pretreatment FMLP (50 $\mu\text{g}/\text{site}$) was injected (i.d.) at 4 different sites, histamine (1 $\mu\text{g}/\text{site}$) and vehicle (100 μl , 1% DMSO v/v in Hanks buffered salt solution) were both injected (i.d.) at 2 different sites.
The responses were allowed to develop for 30 minutes before the animal was sacrificed and a blood sample taken. Skin sites and plasma samples were counted for 1 minute on a gamma counter. The degree of oedema was calculated as μl plasma/skin site. Statistical analysis was carried out by a Mann-Whitney U-test on the mean of the 4 values of μl Plasma obtained for FMLP/animal.

20 The new active compounds can be converted in a known manner into the customary formulations, such as tablets, coated tablets, pills, granules, aerosols, syrups, emulsions, suspensions and solutions, using inert, nontoxic, pharmaceutically suitable excipients or solvents. In this connection, the therapeutically active compound should in each case be present in a concentration of about 0.5 to 90% by weight of the total mixture, i.e. in amounts which are sufficient in order to achieve the dosage range indicated.

25 The formulations are prepared, for example, by extending the active compounds with solvents and/or excipients, if appropriate using emulsifiers and/or dispersants, where, for example, in the case of the use of water as a diluent, organic solvents can be used as auxiliary solvents if appropriate.

Administration is carried out in a customary manner, preferably orally or parenterally, in particular perlingually or intravenously.

In the case of parenteral administration, solutions of the active compound can be employed using suitable liquid vehicles.

30 In general, it has proved advantageous on intravenous administration to administer amounts from about 0.001 to 10 mg/kg, preferably about 0.01 to 5 mg/kg of body weight to achieve effective results, and on oral administration the dosage is about 0.01 to 25 mg/kg, preferably 0.1 to 10 mg/kg of body weight.

35 In spite of this, it may be necessary to depart from the amounts mentioned, in particular depending on the body weight or the type of application route, on individual behaviour towards the medicament, the manner of its formulation and the time or interval at which administration takes place. Thus, in some cases it may be sufficient to manage with less than the abovementioned minimum amount, while in other cases the upper limit mentioned must be exceeded. In the case of administration of relatively large amounts, it is advisable to divide these into several individual doses over the course of the day.

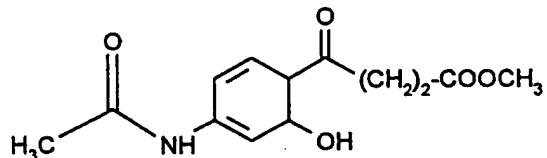
40 Solvents

- I petrolether : ethylacetate 1:1
- II petrolether : ethylacetate 5:1
- III petrolether : ethylacetate 5:2
- 45 IV dichlormethane : methanol 95:5
- V dichlormethane : methanol 5:1
- DMF dimethylformamide

Starting compoundsExample I

- 5 4-Acetamido-2-hydroxy- α -oxo-benzoic acid, methylester

10



15

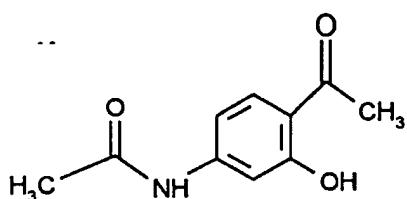
67.5 g (0.41 mol) 3-acetamidoanisole are suspended in 200 ml 1,2-dichloroethane and cooled in an ice bath. 217 g (1.64 mol) AlCl₃ and after it 73.9 g (0.49 mol) 3-carbomethoxypropionylchloride were added successively. Stirring was continued 1/2 hour. After 5 hours the reaction was quenched with ice and ethylacetate and water were added. The organic layer was separated, washed with water, dried over

20 MgSO₄ and concentrated in vacuo. The residue was recrystallized from dioxane and water.
Yield: 52 g (49% of theory)

Example II

N-(4-Acetyl-3-hydroxy-phenyl)-acetamide

30



35

40 67.5 g (0.41 mol) 3-acetamidoanisole are suspended in 200 ml 1,2-dichloroethane and cooled in an ice bath. 217 g (1.64 mol) AlCl₃ and after it 38.5 g (0.49 mol) acetylchloride were added successively. Stirring was continued 1/2 hour. After 5 hours the reaction was quenched with ice and ethylacetate and water were added. The organic layer was separated, washed with water, dried over MgSO₄ and concentrated in vacuo. The residue was recrystallized from dioxane and water. Yield: 39 g (49% of theory)

45

50

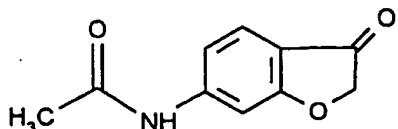
55

Example III

6-Acetylamido-2,3-dihydro-1-benzofuran-3-on

5

10



15 A solution of 10 g (43 mmol) 5-acetylamido-2-(2-chloroacetyl)-phenol and 12 g (140 mmol) sodium acetate in 125 ml ethanol was refluxed over night, cooled to room temperature, followed by addition of 300 ml H₂O. The ethanol was removed under reduced pressure and the residue cooled, filtered and dried. One obtained 8.5 g 6-acetylamido-2,3-dihydro-1-benzofuran-3-on, which was used for the next reaction without further purification.

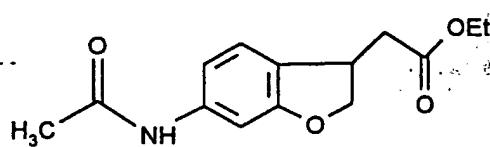
20 ¹H-NMR (200MHz, D₆-DMSO): δ = 2.11 (s, 3H), 4.76 (s, 2H), 7.12 (dd, 1H), 7.57 (d, 1H), 7.72 (d, 1H).
 MSCCI: m/z (%) = 192 (100) [M⁺ + 1]
 R_f = 0.28 (PE/EE = 1:1)

Example IV

25

2-[3-(6-acetylamido-1-benzofuranyl)]ethyl acetate

30



35

A suspension of 224 g (1.17 mmol) III and 490 g (1.4 mmol) (carbethoxymethylene)-triphenylphosphorane in 7.5 l xylene was refluxed over night. Another 389 g (1.17 mmol) (carbethoxymethylenemethylene)-triphenylphosphorane were added and the reaction mixture was refluxed for further 24 hours, concentrated under reduced pressure and the residue suspended in ether. The solids were filtered off and the organic phase concentrated in vacuo.

40 Purification of the crude followed by chromatography (PE/EA 1:1) yielding 115 g (38 %) 2-[3-(6-acetylamido-1-benzofuranyl)]ethyl acetate.

45 ¹H-NMR (250 MHz, CDCl₃): δ = 1.26 (t, 3H), 2.20 (s, 3H), 3.66 (s, 2H), 4.18 (g, 2H), 7.13 (dd, 1H), 7.47 (d, 1H), 7.59 (s, 1H), 7.97 (d, 1H)
 MSCCI, NH₃: m/z (%) = 262 (100) [M⁺ + 1]
 R_f = 0.19 (PE/EE = 1:1).

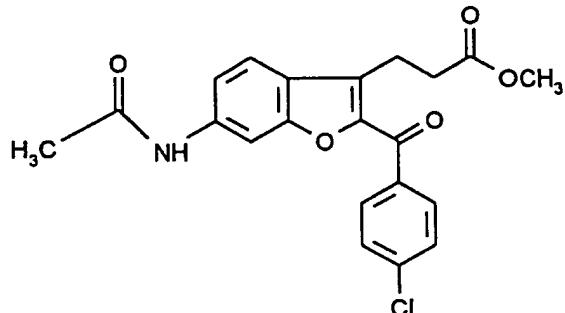
50

55

Preparation ExamplesExample 1

5 3-[6-Acetamido-2-(4-chloro-benzoyl)-3-benzofuranyl]propanoic acid, methylester

10



15

20

25 1.5 g (3.75 mmol) of 2'-Hydroxy-3-oxo-4'-(acetamido)benzenebutanoic acid, methylester and 1.13 g (4.1 mmol) of 2-bromo-4-chloroacetophenone were dissolved in 5 ml DMF and 1.55 g (11.25 mmol) of potassium carbonate were added. The suspension was heated to 60°C for 1h and ethylacetate was added. The organic phase was washed three times with water, one time with a NaCl solution, dried over Na₂SO₄ and concentrated in vacuo. The residue was further purified by crystallisation (ethanol).

30

Yield: 0.75 g (50%)

R_f = 0.12 (III)

The compounds shown in Table 1 were prepared in analogy to the procedure of Example 1:

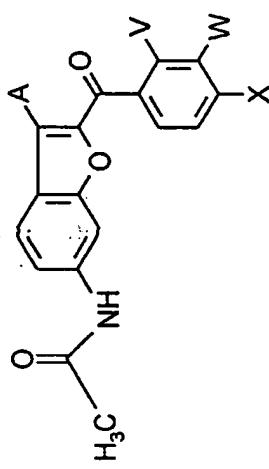
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40

45

50

55

Table 1:

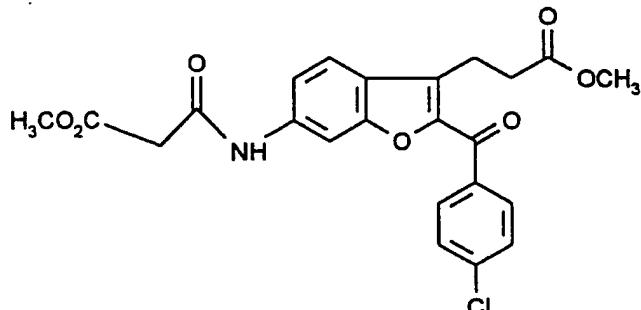
Ex.-No.	V	W	X	A	R _f *	Yield (% of theory)
2	Cl	H	Cl	COOC ₂ H ₅	0,53 (IV)	72
3	H	H	F	CH ₂ CH ₂ COOCH ₃	0,29 (I)	28
4	H	H	CN	CH ₂ CH ₂ COOCH ₃	0,22 (I)	46
5	H	CH ₃	Cl	CH ₂ CH ₂ COOCH ₃	0,23 (I)	66
6	H	H	SCH ₃	CH ₂ CH ₂ COOCH ₃	0,31 (I)	52
7	H	Cl	H	CH ₂ CH ₂ COOCH ₃	0,24 (I)	58
8	H	OCH ₃	H	CH ₂ CH ₂ COOCH ₃	0,18 (I)	68
9	H	H	Cl	COOC ₂ H ₅	0,4 (IV)	20

Example 10

N-[2-(4-Chloro-benzoyl)-3-(2-methoxycarbonyl-ethyl)-benzofuran-6-yl]-malonamic acid methyl ester

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a)

3-[6-Amino-2-(4-chloro-benzoyl)-3-benzofuranyl]propanoic acid, methylester

3.1 g (7.7 mmol) of 2-(4-chloro-benzoyl)-6-acetamido-3-benzofuranylpropanoic acid methylester were suspended in 40 ml methanol. 20 ml 2.6 N HCl were added with stirring. The reaction mixture was heated to reflux. After 1 hour a clear solution was obtained. After 3 hours reflux the solution was cooled to room temperature and ethylacetate was added. The organic layer was washed with NaOH-solution, two times with water, dried over Na₂SO₄ and concentrated in vacuo. The residue was further purified by crystallisation.

Yield: 2.26 g (82%)

R_f: 0.34 (III)

b)

0.5 g (1.4 mmol) of 3-[6-Amino-2-(4-chloro-benzoyl)-3-benzofuranyl]propanoic acid methylester were dissolved in 20 ml methylenechloride and 4 ml triethylamine(Et₃N). 0.6 g (4.5 mmol) (Cl-CO-CH₂-COOCH₃) methylmalonylchloride were added dropwise. The mixture was heated to reflux for 12h. After removing the solvent, ethylacetate and water were added. The organic layer was washed twice with water and NaCl-solution, dried over Na₂SO₄ and concentrated in vacuo. The residue was further purified by recrystallisation (methanol).

Yield: 0.4 g (62.5%)

R_f: = 0.88 (V)

The compounds shown in table 2 were prepared in analogy to the procedure of example 10:

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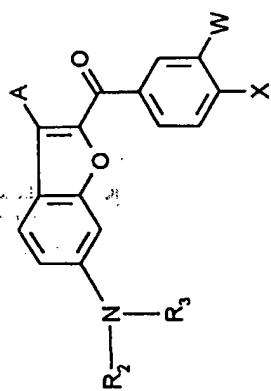
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Table 2:



Ex.-No.	W	X	A	R ²	R ³	R _f [*]	Yield (% of theory)
11	H	Cl	CH ₂ CH ₂ COOCH ₃	COCH ₂ CH ₂ COOCH ₃	H	0,3 (III)	61
12	H	Cl	CH ₂ CH ₂ COOCH ₃	SO ₂ CH ₃	H	0,58 (IV)	12
13	H	Cl	CH ₂ CH ₂ COOCH ₃	SO ₂ CH(CH ₃) ₂	H	0,15 (III)	14
14	H	Cl	CH ₂ CH ₂ CO ₂ CH ₃	SO ₂ C ₂ H ₅	0,1 (II)	58	
15	H	Cl	CH ₂ CH ₂ CO ₂ CH ₃	SO ₂ (CH ₂) ₂ CH ₃	H	0,24 (III)	18
16	H	Cl	CH ₂ CH ₂ CO ₂ CH ₃	SO ₂ C ₆ H ₅	SO ₂ C ₆ H ₅	0,33 (III)	88
17	CN	H	CH ₂ CH ₂ CO ₂ CH ₃	Cl —CO— Cl	H	0,76 (I)	70
18	H	H	CH ₂ CH ₂ CO ₂ CH ₃	-CO-S-C ₂ H ₅	H	0,75 (I)	51

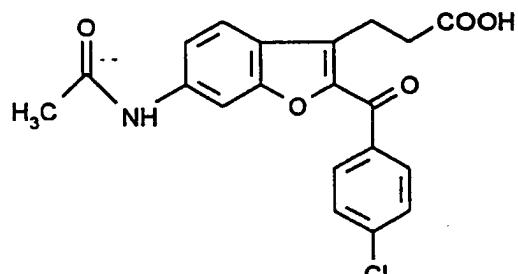
Example 19

3-[6-Acetamido-2-(4-chlorobenzoyl)-3-benzofuranyl]propanoic acid

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20 1.5 g (4.2 mmol) of the compound from starting compounds Example III were dissolved in 50 ml methanol/tetrahydrofuran (1:1) and 5.5 ml of a 2 N NaOH solution were added. The mixture was stirred at r.t. for 24 hours, dissolved in water and acidified with 1 N hydrochloric acid. The precipitate was filtered off, washed several times with water and dried in vacuo. The further reaction was carried out as described in Example 1.

25 Yield: 96%
R_f: 0.54 (V)

30 The compounds shown in Table 3 were prepared in analogy to the procedure of Example 19:

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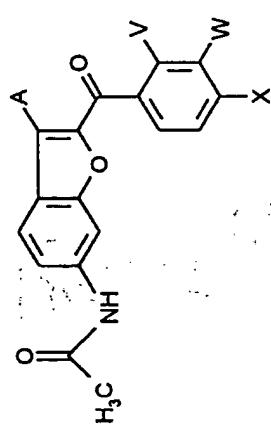
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Table 3

Ex.-No.	V	W	X	A	R _f *	Yield ; (% of theory)
20	H	H	Cl	CH ₂ CH ₂ CO ₂ Na	0,58 (IV)	98
21	H	H	SCH ₃	CH ₂ CH ₂ COOH	0,68 (V)	88
22	H	H	F	CH ₂ CH ₂ COOH	0,51 (V)	83
23	H	Cl	H	CH ₂ CH ₂ COOH	0,51 (V)	95
24	H	OCH ₃	H	CH ₂ CH ₂ COOH	0,54 (V)	87

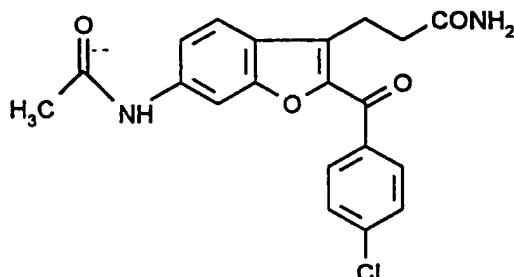
Example 25

3-[6-Acetamido-3-(2-carbonamid-ethyl)-2-(4-chloro-benzoyl)-benzofuran

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20 0.56 g (1.3 mmol) of the acid from example 1 were dissolved in 5 ml THF, 0.25 g (1.25 mmol) 1,1'-carbonyl-bis-1H-imidazole were added and the mixture was stirred at room temperature for 12 hours. Subsequently NH₃-gas was added for 2 h using an inlet pipe. After one additional hour stirring at r.t. the solvent was distilled off in vacuo. The residue was taken up in ethylacetate and washed three times with water, one time with a NaHCO₃ solution and one time with a NaCl solution. The organic phase was dried over MgSO₄ and the solvent was removed in vacuo.

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Yield: 83%

R_f: 0.72 (V)Example 26

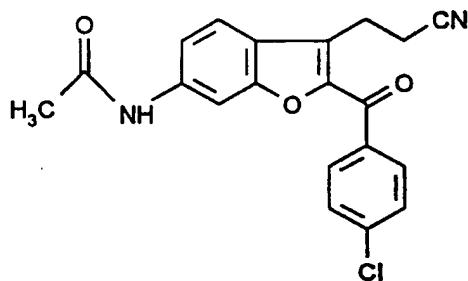
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3-[6-Acetamido-2-(4-chloro-benzoyl)-3-(2-cyano-ethyl)-benzofuran

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50 0.56 g (1.3 mmol) of example 25 were dissolved in 15 ml dioxane. 0.2 ml (2.6 mmol) pyridine were added, cooled to 5-10°C and 0.22 ml (1.56 mmol) trifluoroacetic anhydride were added dropwise. The mixture was stirred for 3 hours at room temperature. The mixture was added to water, washed twice with dichloromethane. The organic layer was dried and the solvent removed in vacuo.

Yield: 73%

R_f: 0.49 (IV)

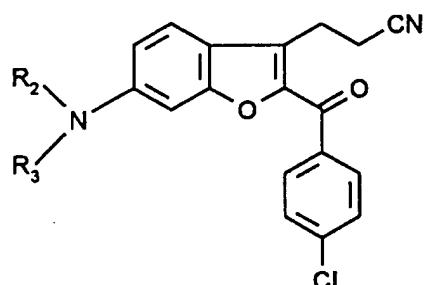
55 The compounds shown in Table 4 were prepared in analogy to the procedure of Example 26:

Table 4:

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Ex.-No.	R ²	R ³	R _f *	Yield (% of theory)
27	CH ₃ SO ₂ ⁻	H	0,66 (IV)	40
28	CH ₃ SO ₂ ⁻	CH ₃ SO ₂ ⁻	0,7 (IV)	55

The compounds shown in Table 5 are prepared by Friedel-Crafts Reaction of Example IV.

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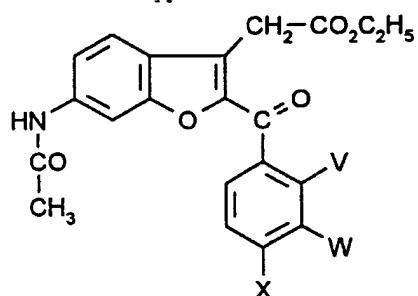
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Table 5

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Example No.	V	W	X	R _f *	yield (% of theory)
29	H	H	-C ₄ H ₉	0.22 (I)	31
30	H	H	-CH ₃	0.21 (I)	86
31	H	H	-C ₆ H ₅	0.5 (IV)	70
32	Cl	H	-Cl	0.6 (IV)	97
33	H	H	-Br	0.25 (I)	76
34	H	Br	H	0.33 (II)	68
35	H	CN	H	0.25 (I)	75

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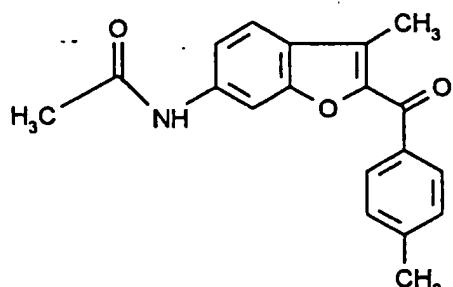
Example 36

N-[3-Methyl-2-(4-methyl-benzoyl)-benzofuran-6-yl]acetamide

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20 0.72 g (3.75 mmol) of N-(4-acetyl-3-hydroxy-phenyl)acetamide and 0.81 g (4.1 mmol) of 2-bromo-4-methylacetophenone were dissolved in 5 ml DMF and 1.55 g (11.25 mmol) of potassium carbonate were added. The suspension was heated to 60°C for 1 h and ethylacetate was added. The organic phase was washed three times with water, one time with a NaCl solution, dried over Na₂SO₄ and concentrated in vacuo. The residue was further purified by crystallisation (ethanol).

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Yield: 0.58 g (50%)

R_f = 0.12 (III)

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The compounds shown in Table 6 were prepared in analogy to the procedure of Example 36:

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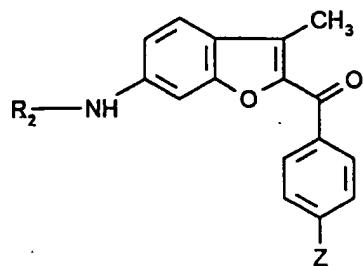
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Table 6:

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Ex.-No.	Z	R ²	R _f *	Yield (% of theory)
37	CH ₃	CO ₂ CH ₃	0.64 (IV)	87
38	CH ₃	CHO	0.91 (IV)	64
39	CH ₃	CH ₂ CO ₂ C ₂ H ₅	0.69 (IV)	20
40	Cl	COCH ₃	0.33 (IV)	38
41	C ₆ H ₅	COCH ₃	0.35 (I)	53

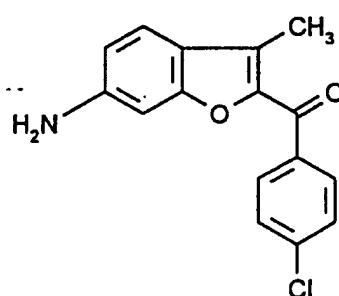
Example 42

40 (6-Amino-3-methyl-benzofuran-2-yl)-(4-chlorophenyl)-methanone

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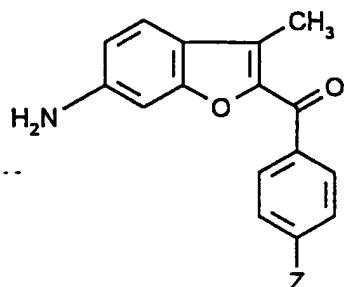
3.1 g (10 mmol) of N-[3-methyl-2-(4-methyl-benzoyl)benzofuran-6-yl]-acetamide were suspended in 40 ml methanol. 20 ml 2.6 N HCl were added with stirring. The reaction mixture was heated to reflux. After 1 hour a clear solution

was obtained. After 3 hours reflux the solution was cooled to room temperature and ethylacetate was added. The organic layer was washed once with NaOH-solution, two times with water, dried over Na_2SO_4 and concentrated in vacuo. The residue was further purified by crystallisation.

5 Yield: 2,2 g (83%
 R_f : 0.7 (IV)

The compounds shown in Tables 7 and 8 were prepared in analogy to the procedure of example 42:

10 **Table 7:**



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Ex.-No.	Z	R_f^*	Yield (% of theory)
43	CH_3	0.62 (IV)	87
44	C_6H_5	0.38	71

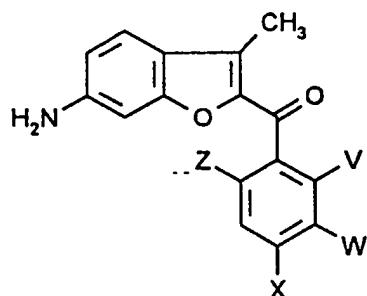
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Table 8

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Example No.	X	V	Z	W	R _f	yield
45	CH ₃	CH ₃	CH ₃	H	0.98 (IV)	70
46	Br	H	H	H	0.45 (I)	55
47	NO ₂	H	H	H	0.83 (I)	22
48	H	H	H	CN	0.38 (IV)	92
49	CN	H	H	H	0.77 (I)	70
50	Cl	Cl	H	H	0.26 (I)	65
51	H	H	H	NO ₂	0.79 (I)	88
52	H	H	H	Br	0.27 (I)	71
53	H	H	H	OCH ₃	0.21 (I)	96
54	H	H	H	CH ₃	0.25 (I)	73
55	H	H	H	CF ₃	0.35 (I)	37
56	-C ₆ H ₄ -OCH ₃	H	H	NO ₂	0.37 (II)	40

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The compounds shown in Table 9 were prepared in analogy to the procedure of example 36

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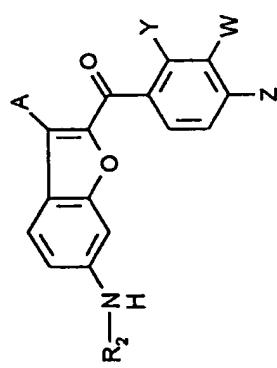
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**Table 9:**

Example No.	Y	Z	W	R ²	A	R _f	yield
57	H	C ₆ H ₅	H	CONH ₂	CH ₃	0.18 (I)	76
58	H	NO ₂	H	COCH ₃	CH ₃	0.28 (I)	63
59	H	Br	H	COCH ₃	CH ₃	0.32 (I)	73
60	H	H	CN	COCH ₃	CH ₃	0.47 (IV)	29
61	H	CN	H	COCH ₃	CH ₃	0.27 (I)	13
62	Cl	Cl	H	COCH ₃	CH ₃	0.4 (I)	46

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Table 9: (continuation)

Example No.	Y	Z	W	R ²	A	R _f	yield
63	H	H	NO ₂	COCH ₃	CH ₃	0.29 (I)	16
64	H	H	Br	COCH ₃	CH ₃	0.37 (I)	43
65	H	H	OCH ₃	COCH ₃	CH ₃	0.29 (I)	76
66	H	H	CH ₃	COCH ₃	CH ₃	0.13 (III)	58
67	H	H	CF ₃	COCH ₃	CH ₃	0.13 (III)	35
68	H		NO ₂	COCH ₃	CH ₃	0.24 (I)	7
69	H	CH ₃	H		CH ₃	0.18 (III)	30
70	H	CH ₃	H		CH ₃	0.22 (III)	35

Table 9: (continuation)

Example No.	Y	Z	W	R ²	A	R _f	yield
71	H	CH ₃	H		CH ₃	0.08 (II)	40
72	H	CH ₃	H		CH ₃	0.02 (III)	42
73	H	CH ₃	H		CH ₃	0.12 (III)	30
74	H	CH ₃	H		CH ₃	0.26 (II)	35
75	H	CH ₃	H		CH ₃	0.26 (III)	40

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Table 9: (continuation)

Example No.	Y	Z	W	R ²	A	R _f	yield
76	H	CH ₃	H		CH ₃	0.12 (III)	30
77	H	CH ₃	H		CH ₃	0.26 (II)	35

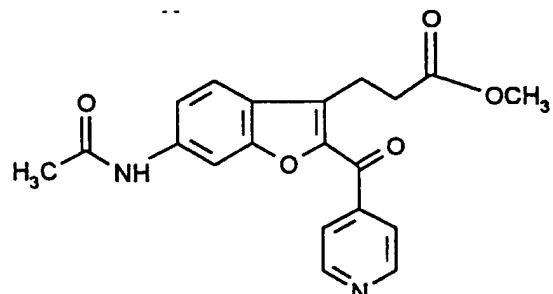
Example 78

3-[6-Acetylamino-2-(pyridine-4-carbonyl)-3-benzofuranyl]propanoic acid, methylester

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20 1.5 g (3.75 mmol) of 2'-Hydroxy-3-oxo-4'[(acetamido)]benzenebutanoic acid, methylester and 0.82 g (4.1 mmol) of 2-bromo-1-(4-pyridyl)-ethanone were dissolved in 5 ml DMF and 1.55 g (11.25 mmol) of potassium carbonate were added. The suspension was heated to 50°C for 1 h, ethylacetate was added. The organic phase was washed three times with water, one time with a NaCl solution, dried over Na₂SO₄ and concentrated in vacuo. The residue was further purified by chromatography.

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Yield: 0.412 g (30%)

R_f = 0.1, (I)

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The compounds shown in Table 10 were prepared in analogy to the procedure of Example 78:

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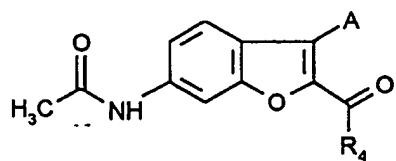
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Table 10:

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Ex.-No.	A	R ⁴	R _f *	Yield (% of theory)
79	-COOC ₂ H ₅		0,1 (I)	30
80	-CH ₂ CH ₂ CO ₂ CH ₃		0,32 (IV)	72

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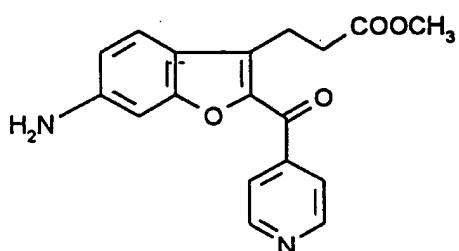
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Example 81

40 3-[6-Amino-2-(chloro-4-benzoyl)-3-benzofuranyl]propanoic acid, methylester

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55 2.8 g (7.7 mmol) of 2-(4-chloro-benzoyl)-6-acetamido-3-benzofuranpropanoic acid methylester were suspended in 40 ml methanol. 20 ml 2.6 N HCl was added with stirring. The reaction mixture was heated to reflux. After 1 hour a clear solution was obtained. After 3 hours reflux the solution was cooled to room temperature and ethylacetate added. The organic layer was washed with NaOH-solution, two times with water, dried with Na₂SO₄ and concentrated in vacuo. The

residue was further purified by crystallisation.

Yield: 1.64 g (60%)

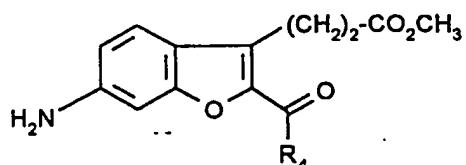
R_f: 0.34 (III)

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The compounds shown in Table 11 were prepared in analogy to the procedure of example 81:

Table 11:

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Ex.-No.	R ⁴	R _f *	Yield (% of theory)
82		0.6 (V)	90
83		0.32 (IV)	50
84		0.4 (IV)	75

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The compounds shown in Table 12 were prepared in analogy to the procedure of example 78.

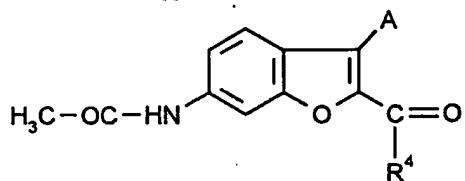
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Table 12:

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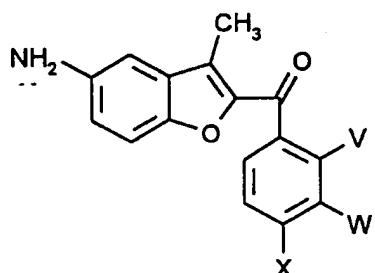
Example No.	A	R ⁴	R _f *	yield
85	C ₂ H ₄ COOCH ₃		0.25 (IV)	30
86	C ₂ H ₄ COOCH ₃		0.3 (IV)	20
87	CH ₃		0.34 (IV)	63

The compounds shown in the Tables 13 and 14 are prepared in analogy to the procedure of 42.

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Table 13:

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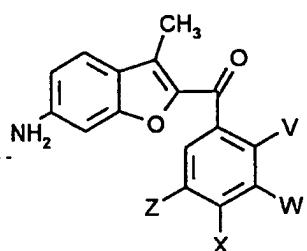
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Example No.	V	W	X	R _f *	yield (% of theory)
88	H	H	F	0.5 (I)	98
89	H	H	Br	0.5 (III)	97
90	H	H	C ₂ H ₅	0.44 (I)	82
91	H	H		0.5 (I)	82
92	Cl	H	Cl	0.63 (I)	80
93	H	NO ₂	H	0.5 (I)	70
94	H	CH ₃	H	0.63 (I)	94
95	CH ₃	H	CH ₃	0.91 (I)	81
96	H	H	NO ₂	0.83 (I)	77
97	H	CF ₃	H	0.69 (I)	91
98	H	OCH ₃	H	0.66 (I)	90
99	H		H	0.42 (I)	94

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Table 14

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Ex. No.	V	W	X	Z	R _f *	yield (% of theory)
100	H		H	H	0.63 (I)	100
101	H	H	C ₉ H ₁₉	H	0.84 (V)	78
102	H	H	C ₆ H ₁₃	H	0.80 (V)	76
103	H	H		H	0.7 (V)	97
104	H		H	H	0.66 (III)	93
105	H		H	H	0.72 (III)	78
106	H		H	H	0.85 (V)	95
107	H		H	H	0.87 (V)	100

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Table 14: (continuation)

Ex. No.	V	W	X	Z	R _f *	yield (% of theory)
108	H	H	COOH	H		
109	H	H	F	H	0.77 (IV)	77
110	H	H	C ₂ H ₅	H	0.84 (IV)	78
111	H	H		H	0.9 (IV)	65
112	H	H	OCH ₃	H	0.371 (I)	92
113	OCH ₃	H	OCH ₃	H	0.257	88.3
114	H	H	OH	H	0.27 (IV)	43
115	H	H		H	0.85 (IV)	80
116	H	H	NO ₂	H	0.79 (I)	88
117	H	H	Br	H	0.78 (I)	58
118	H	H	OCH ₃	H	0.75 (I)	93
119	Cl	Cl	H	H	0.79 (I)	40
120	H	H	CH ₃	H	0.34 (I)	76
121	H	H	CF ₃	H	0.41 (I)	97
122	H		NO ₂	H	0.53 (I)	40
123	CH ₃	CH ₃	H	H	0.98 (I)	91
124	H		H	H	0.53 (I)	19

Table 14: (continuation)

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Ex. No.	V	W	X	Z	R _f *	yield (% of theory)
125	H	H		H	0.72 (I)	78

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The compounds shown in Tables 15, 16, 17, 18, 19 and 20 are prepared in analogy to the procedure of example 1. Compounds with ethylacetate substituted in position A are prepared by Friedel-Crafts reaction of Example IV with aryl acid chloride.

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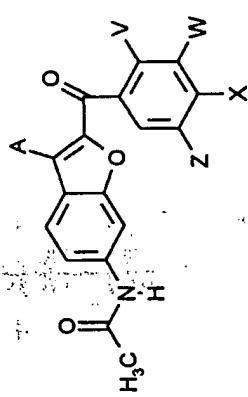
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Table 15:

Example No.	V	W	X	Z	A	R _f *	yield (% of theory)
126	H	H	CH ₃	H	—	0.59 (IV)	15
127	H	CN	H	H	—	0.5 (IV)	76
128	H	H	F	H	—	0.46 (I)	70
129	H	H	—	cyclohexyl	—	0.52 (I)	87

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Table 15: (continuation)

Example No.	V	W	X	Z	A	R _f [*]	yield (% of theory)
130	H	H		H		0.55 (I)	100
131	H	H	F	H		0.5 (I)	89
132	H	H	NO ₂	H	CH(CH ₃) ₂	0.5 (I)	30
133	H	H	CH ₃	H	CH(CH ₃) ₂	0.5 (I)	77
134	H	OCH ₃	H	H	CH(CH ₃) ₂	0.5 (I)	65
135	Cl	H	Cl	H	CH(CH ₃) ₂	0.53 (I)	68
136	CH ₃	H	CH ₃	H	CH(CH ₃) ₂	0.53 (I)	86
137	H	H	CF ₃	H	CH(CH ₃) ₂	0.53 (I)	63
138	H	H	CH ₃	H		0.41 (I)	61
139	H	Br	H	H	OH	0.69 (IV)	25

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Table 15: (continuation)

Example No.	V	W	X	Z	A	R _f *	yield (% of theory)
140	H	-OCH ₃	H	H		0.48 (I)	57
141	H	H	CH ₃	H	-OH	0.53 (V)	52
142	H	H	CH ₃	H	H	0.21 (I)	59
143	H	-OCH ₃	H	H	-C ₂ H ₅	0.37 (III)	:44
144	H	-OCH ₃	H	H		0.42 (I)	51
145	H	H	CH ₃	H	-OC ₂ H ₅	0.43 (I)	31
146	H	CF ₃	H	H		0.55 (I)	68
147	Cl	H	Cl	H		0.54 (I)	57
148	H	CF ₃	H	H		0.41 (I)	65
149	H	Br	H	H		0.44 (I)	72

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Table 15: (continuation)

Example No.	V	W	X	Z	A	R_f^*	yield (% of theory)
150	Cl	H	Cl	H		0.62 (I)	46
151	H	CH ₃	H	H	-C ₂ H ₅	0.51 (I)	54
152	H	CH ₃	H	H		0.53 (I)	77
153	H	H	Cl	H	CH ₂ CO ₂ Et	0.46 (V)	44
154	H	H	OCH ₃	H	CH(CH ₃) ₂	0.08 (III)	79
155	-OCH ₃	H	OCH ₃	H	CH(CH ₃) ₂	0.08 (III)	83
156	OCH ₃	H	OCH ₃	H		0.13 (I)	48.5
157	H	H	OCH ₃	H		0.26 (I)	49.1
158	H	H	Br	H		0.28 (I)	13

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Table 15: (continuation)

Example No.	V	W	X	Z	A	R _f * 0.44 (I)	yield (% of theory) 31
159	H	H		H			
160	H	Br	H	H	C ₂ H ₅	0.3 (III)	27
161	H	H	CN	H	C ₂ H ₅	0.6 (IV)	45
162	H	CN	H	H	C ₂ H ₅	0.6 (IV)	26
163	H	H	C ₂ H ₅	H	C ₂ H ₅	0.67 (IV)	58
164	H	H		H	C ₂ H ₅	0.44 (I)	74
165	H	H	F	H	C ₂ H ₅	0.07 (III)	65
166	H	H	Br	H	CH(CH ₃) ₂	0.3 (I)	67
167	H	Br	H	H	CH(CH ₃)	0.32 (I)	31
168	H	H	CN	H	CH(CH ₃)	0.65 (IV)	38
169	H	CN	H	H	CH(CH ₃) ₂	0.63 (IV)	59

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Table 15: (continuation)

Example No.	V	W	X	Z	A	R _f [*]	yield (% of theory)
170	H	H	C ₂ H ₅	H	CH(CH ₃) ₂	0.2 (III)	88
171	H	H		H	CH(CH ₃) ₂	0.2 (III)	75
172	H	H	F	H	CH(CH ₃) ₂	0.15 (III)	93
173	H	H		H	CH(CH ₃) ₂	0.4 (I)	86
174	H	H	-(CH ₂) ₃ CH ₃	H	-CH ₂ CO ₂ C ₂ H ₅	0.55	68.6
175	H	H		H	-CH ₂ CO ₂ C ₂ H ₅	0.358	70.6
176	H	H	Br	H	CH ₂ CH ₃	0.133	67
177	H	H		H	CH ₂ CH ₃	0.29	66

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Table 15: (continuation)

Example No.	V	W	X	Z	A	R _f *	yield (% of theory)
178	H	H		H		0.42	31
179	H	H		H		0.22	28.4
180	H	H		H		0.15	89.2
181	H	H		H		0.32	70.9
182	H	H	OCH ₃	H		0.29	58.4
183	OCH ₃	H	OCH ₃	H		0.29	67.2

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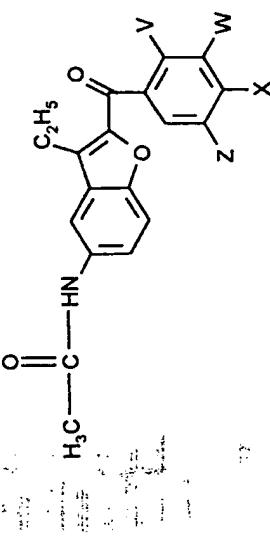
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Table 15: (continuation)

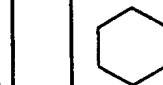
Example No.	V	W	X	Z	A	R_f^*	yield (% of theory)
184	H	H	Br	H	—○—	0.38	77.6

Table 16:



Example No.	V	W	X	Z	R _f *	yield (% of theory)
185	Cl	H	Cl	H	0.51 (I)	59
186	H	CH ₃	H	H	0.60 (I)	53
187	H	OCH ₃	H	H	0.43 (I)	47
188	H	CF ₃	H	H	0.53 (I)	42
189	H	NO ₂	H	H	0.42 (I)	12
190	H	H	OCH ₃	H	0.58	97
191	H	H		H	0.45	68

Table 16: (Continuation)

Example No.	V	W	X	Z	R _f *	yield (% of theory)
192	H	H	C ₂ H ₅	H	0.56 (IV)	63
193	H	H	CH ₃	H	0.27 (I)	86
194	H	H		H	0.35 (I)	79

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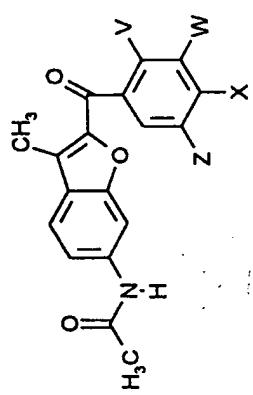
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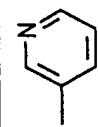
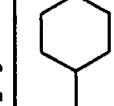
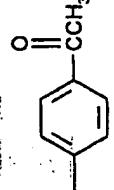
Table 17:

Example No.	V	W	X	Z	R _f *	yield (% of theory)
195	H		H	H	0.39 (I)	65
196	H	H	C ₉ H ₁₉	H	0.06 (III)	57
197	H	H	C ₆ H ₁₃	H	0.42 (V)	35
198	H	H		H	0.66 (V)	67
199	H	CH ₃		H	0.48 (V)	83

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Table 17: (continuation)

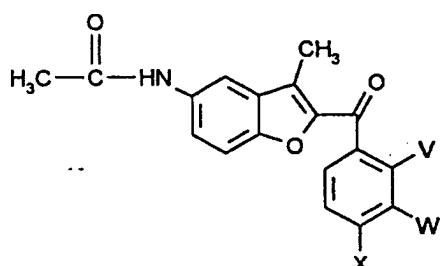
Example No.	V	W	X	Z	R _f *	yield (% of theory)
200	H		H	H	0.68 (V)	97
201	H	H	F	H	0.8 (I)	98
202	H	H	C ₂ H ₅	H	0.5 (IV)	50
203	H	H		H	0.6 (IV)	71
204	H	H	OCH ₃	H	0.2 (IV)	63
205	OCH ₃	H	OCH ₃	H	0.2 (IV)	62
206	CH ₃	H	CH ₃	H	0.4 (I)	51
207	H	H		H	0.2 (I)	21

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Table 17: (continuation)

Example No.	V	W	X	Z	R _f *	yield (% of theory)
208	H		H	H	0.32 (I)	68
209	H	H	OH	H	0.14 (I)	20
210	H	H		H	0.2 (IV)	61
211	H	H		H	0.47 (IV)	30
212	H	H	Br	H	0.65	60
213	H	H		H	0.1	76

Table 18:

Example No.	V	W	X	R _f *	yield (% of theory)
214	H	H	F	0.5 (IV)	83
215	H	H	Br	0.45 (III)	68
216	H	H	C ₂ H ₅	0.48 (IV)	60
217	H	H		0.54 (IV)	78
218	H	Br	H	0.27 (I)	71
219	Cl	H	Cl	0.26 (I)	65
220	H	NO ₂	H	0.15 (I)	20
221	H	CH ₃	H	0.25 (I)	73
222	CH ₃	H	CH ₃	0.36 (I)	57
223	H	H	NO ₂	0.19 (I)	16
224	H	CF ₃	H	0.35 (I)	37
225	H	OCH ₃	H	0.21 (I)	96
226	H	H		0.26 (I)	81

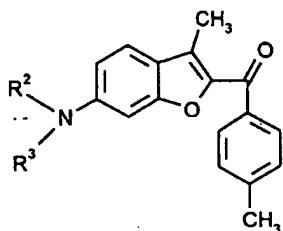
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Table 19:

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Example No.	R ²	R ³	R _f *	yield (% of theory)
227	-CH ₂ CO ₂ Et	-CH ₂ CO ₂ Et	0.21 (III)	79
228	-CH ₂ CO ₂ H	-CH ₂ CO ₂ H	0.03 (II)	98
229	H	-COCH ₂ OCH ₃	0.6 (II)	85

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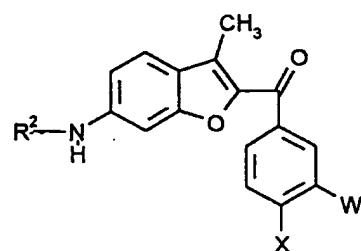
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Table 20:

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Example No.	R^2	X	W	R_f^*	yield (% of theory)
230	$-\text{COCH}_2\text{OCH}_3$	CH_3	H	0.6 (III)	85
231	$-\text{COCH}_3$	H		0.64 (V)	55
232	$-\text{COCH}_3$	H		0.75 (V)	31
233	$-\text{SO}_2\text{NHC}(\text{CH}_3)_3$	CH_3	H	0.72 (III)	58
234	$-\text{SO}_2\text{NH}_2$	CH_3	H	0.64 (III)	70
235	$-\text{COCH}_2\text{OCOCH}_3$	CH_3	H	0.58 (III)	70
236	$-\text{COCH}_2\text{OH}$	CH_3	H	0.4 (III)	79
237		CH_3	H		

The compounds shown in Tables 21 to 24 are prepared in analogy to the abovementioned procedures.

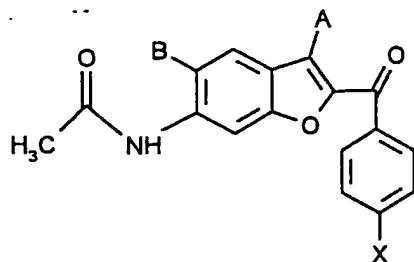
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Table 21:

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Ex.-No.	B	X	A	R _f *	yield in %
238	H	CH ₃	—	0.46 (IV)	88
239	H	CH ₃	-C ₂ H ₅	0.35 (IV)	85
240	H	Cl	-CH ₂ CO ₂ Et	0.91 (IV)	12
241	H		-C ₂ H ₅	0.09 (I)	63
242	H		-CH(CH ₃) ₂	0.17 (I)	28.5
243	H	H	—	0.41 (IV)	91
244	H		-CH ₃	0.34 (IV)	76
245	H	Cl	—	0.39 (IV)	57

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Table 21: (Continuation)

Ex.- No.	B	X	A	R _f *	yield in %
246	H	-C ₂ H ₅		0.47 (IV)	73
247	H	Cl	-OH	0.30 (IV)	52
248	H	F	-CH(CH ₃) ₂	0.25 (IV)	93
249	CH ₃	CH ₃	-CH ₃	0.28 (I)	53

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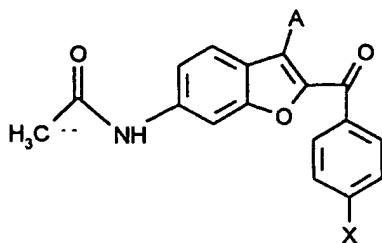
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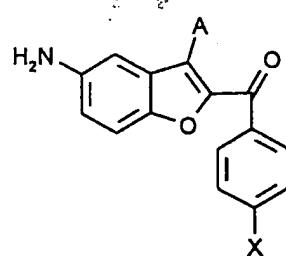
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Table 22:

Ex.-No.	X	A	R _f *	yield
250	CH ₃	CH ₃	0.43 (IV)	84
251	CN	CH ₃	0.20 (IV)	42
252	H	CH ₃	0.47 (IV)	14
253	NO ₂	CH ₃	0.21 (I)	16
254	F	C ₂ H ₅	0.44 (IV)	quant.

Table 23:

Ex.-No.	X	A	R _f *	yield (% of theory)
255	CH ₃	CH ₃	0.73 (IV)	97
256	H	CH ₃	0.85 (IV)	84
257	-CN	CH ₃	0.52 (IV)	95

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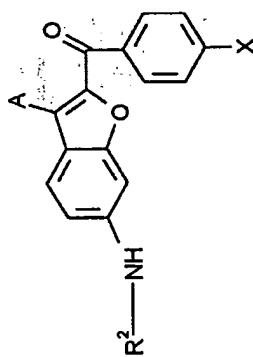
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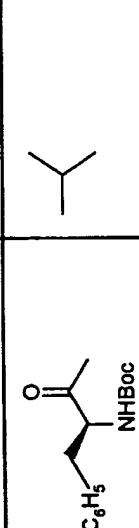
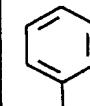
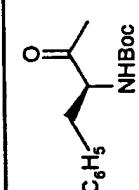
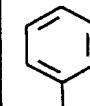
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Table 24:

Ex.-No.	R ²	A	X	R _f *	yield (% of theory)
258	C ₆ H ₅		Br	0.65 (IX)	73
259			Br	0.68 (X)	53.8

Ex.-No.	R ²	A	X	R _f *	yield (% of theory)
260				0.68 (IX)	67
261				0.66 (X)	86

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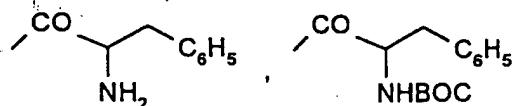
Claims

1. Amino-benzofuryl- and thiienyl-derivatives of the general formula (I) in which

I.:

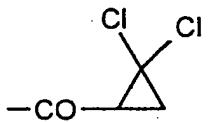
- 5 R¹ represents hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms or
represents halogen, carboxyl, cyano, nitro, trifluoromethyl or a group of a formula -OR⁵, -
SR⁶ or -NR⁷R⁸,
in which
- 10 R⁵, R⁶ and R⁸ are identical or different and denote hydrogen, cycloalkyl having 3 to 6 carbon atoms, benzyl or a 5 to 7-membered saturated or unsaturated heterocycle having up to 4 heteroatoms from the series comprising N, S and/or O and to which a phenyl ring can be fused and which is optionally substituted by identical or different substituents from the series comprising halogen, cyano, nitro or by a straight-chain or branched alkyl having up to 6 carbon atoms or
- 15 denote straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, or
denote phenyl, which is optionally monosubstituted to disubstituted by identical or different substituents from the series comprising nitro, halogen, carboxy or straight-chain or branched alkoxy carbonyl having up to 6 carbon atoms,
or
- 20 R⁵ denotes a hydroxyl protecting group, from the series comprising trimethylsilyl, t-butyl-dimethylsilyl, benzyl, 4-nitrobenzyl, 4-methoxybenzyl, acetyl, tetrahydropyranyl and benzoyl,
- 25 R⁷ denotes hydrogen or a straight-chain or branched alkyl having up to 4 carbon atoms,
R² represents formyl or straight-chain or branched acyl, alkoxy or alkoxy carbonyl each having up to 8 carbon atoms in the alkyl group,
or represents benzoyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising halogen, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl each having up to 6 carbon atoms in the alkyl group,
or represents a group of a formula

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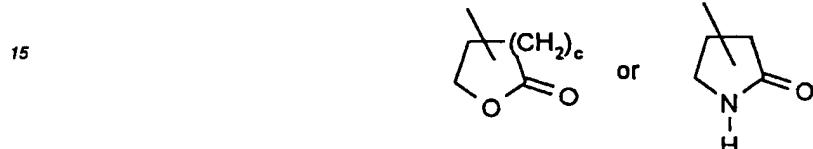
-SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO-(CH₂)_b-R¹², -CO-S-R¹³ or a residue of the formula



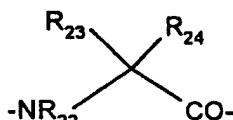
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- R⁹ in which
denotes straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by phenyl, or
denotes phenyl, which is optionally substituted by trifluoromethyl, cyano, nitro or straight-chain or branched alkyl having up to 6 carbon atoms,
- 50 R¹⁰ and R¹¹ are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms or phenyl,
R¹² denotes straight-chain or branched hydroxyl, oxyacyl, alkoxy or alkoxy carbonyl each having up to 6 carbon atoms or carboxy,
- 55 a denotes a number 0, 1, 2 or 3,
b denotes a number 1, 2 or 3,
R¹³ denotes straight-chain or branched alkyl having up to 6 carbon atoms,
R³ represents hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, or

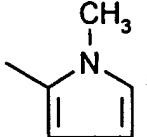
has the abovementioned meaning of R²,
 T represents an oxygen or sulfur atom
 A represents hydrogen, hydroxyl, cycloalkyl with 3 to 6 carbon atoms, carboxy or straight-chain or branched alkoxy carbonyl or alkoxy each having up to 6 carbon atoms, or straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms and each of which is optionally monosubstituted by cyano or by a 5 to 7-membered saturated or unsaturated heterocycle having up to 4 heteroatoms from the series comprising N, S and O, which is optionally substituted by identical or different substituents from the series comprising hydroxy, halogen, cyano, nitro or by a straight-chain or branched alkyl having up to 6 carbon atoms,
 10 or alkyl or alkenyl are optionally substituted by a group of a formula



20 in which
 C denotes a number 1 or 2, and in which both rings are optionally monosubstituted by hydroxy, halogen or by straight-chain or branched alkyl having up to 6 carbon atoms,
 25 or alkyl or alkenyl are optionally monosubstituted by a group of a formula -CO-R¹⁴, -CO-NR¹⁵R¹⁶, -CONR¹⁷-SO₂-R¹⁸ or -PO(OR¹⁹)(OR²⁰), -OR²¹ or



35 R¹⁴ in which
 denotes hydroxyl, cycloalkyloxy having 3 to 7 carbon atoms or straight-chain or branched alkyl or alkoxy each having up to 8 carbon atoms,
 R¹⁵, R¹⁶ and R¹⁷ are identical or different and represent hydrogen, straight-chain or branched alkyl having up to 6 carbon atoms, phenyl or benzyl,
 or
 40 R¹⁵ denotes hydrogen,
 and
 R¹⁶ denotes hydroxyl,
 or
 45 R¹⁵ and R¹⁶ together with the nitrogen atom form a 5-or 6-membered saturated heterocycle,
 R¹⁸ denotes a straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by phenyl or trifluoromethyl,
 or
 denotes phenyl, which is optionally substituted by substituents from the series comprising halogen, cyano, nitro or by a straight-chain or branched alkyl having up to 6 carbon atoms,
 50 R¹⁹, R²⁰ and R²¹ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms,
 R²² denotes hydrogen, an aminoprotecting group or straight-chain or branched alkyl having up to 6 carbon atoms,
 55 R²³ and R²⁴ are identical or different and denote hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,
 or
 R²³ has the abovementioned meaning,
 and

- 24 R²⁴ denotes cycloalkyl having 3 to 6 carbon atoms or aryl having 6 to 10 carbon atoms or straight-chain or branched alkyl having up to 8 carbon atoms, which is optionally substituted by cyano, methythio, hydroxy, mercapto, guanidyl or a group of a formula - NR²⁵R²⁶ or R²⁷-CO-,
 5 wherein
 R²⁵ and R²⁶ have the meaning shown above for R¹⁵, R¹⁶ and R¹⁷,
 R²⁷ denotes hydroxyl, benzyloxycarbonyl, straight-chain or branched alkoxy having up to 6 carbon atoms or the abovementioned group -NR²⁵R²⁶,
- 10 or alkyl is optionally substituted by cycloalkyl having 3 to 6 carbon atoms, or by aryl having up to 10 carbon atoms, which is optionally substituted by hydroxyl, halogen, nitro, straight-chain or branched alkoxy having up to 8 carbon atoms or by the abovementioned group of the formula -NR²⁵R²⁶,
 or alkyl is optionally substituted by indolyl or by a 5 to 6 membered unsaturated heterocycle having up to 4 N-atoms wherein optionally all -NH-functions are protected by straight-chain or branched alkyl having up to 6 carbon atoms or by an amino protecting group,
 15 and
- 10 R⁴ represents phenyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, adamantyl, phenoxy, cycloalkyl having up to 6 carbon atoms, halogen, nitro, furanyl, thiienyl, pyridyl, tetrazolyl, trifluoromethyl, difluoromethyl, cyano, carboxyl, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 11 carbon atoms in the alkyl group or by phenyl, which is optionally monosubstituted to trisubstituted by nitro, halogen, formyl, carbonyl or straight chain or branched alkoxy, acyl, alkoxy carbonyl or alkyl each having up to 6 carbon atoms, which is optionally substituted by hydroxyl
 20 or phenyl is substituted by a group of formula - NR²⁸R²⁹, -SR³⁰, SO₂R³¹,
 -O-SO₂R³² or
- 25 30 
- 35 R²⁸ and R²⁹ in which
 40 have the meaning shown above for R¹⁰ and R¹¹,
 R²⁸ or
 denotes hydrogen,
 and
 R²⁹ denotes straight-chain or branched acyl having up to 6 carbon atoms,
 R³⁰ denotes straight-chain or branched alkyl having up to 6 carbon atoms,
 45 R³¹ and R³² are identical or different and represent straight-chain or branched alkyl having up to 6 carbon atoms, benzyl or phenyl, which are optionally substituted by trifluoromethyl, halogen or straight-chain or branched alkyl having up to 6 carbon atoms,
 with the proviso that A does not denote methyl
 or
- 50 II. : if A represents a methyl group
- 55 R¹, T and R⁴ have the meaning described in part I,
 and in this case
 R² and R³ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, or
 represent formyl or straight-chain or branched acyl, alkoxy or alkoxy carbonyl each having up to

8 carbon atoms,
or represent benzoyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising halogen, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl each having up to 6 carbon atoms,

5 or represent a group of a formula $-\text{SO}_2(\text{NH})_8\text{R}^{33}$, SO_2NH_2 ,
 $-\text{CO}-(\text{CH}_2)_d\text{NR}^{34}\text{R}^{35}$, $-(\text{CH}_2)_e\text{-CO-R}^{36}$, $-\text{CO}-(\text{CH}_2)_f\text{R}^{37}$ or $-\text{CO-X}$,
in which

10 R^{33} has the abovementioned meaning of R^9 and is identical or different to the latter,
 R^{34} and R^{35} are identical or different and have the abovementioned meaning of R^{10} and R^{11} ,

15 R^{36} denotes hydroxyl or straight-chain or branched alkoxy having up to 6 carbon atoms,
 R^{37} has the abovementioned meaning of R^{12} or denotes straight-chain or branched alkoxy or oxy-

acyl each having up to 6 carbon atoms or hydroxyl.

d has the abovementioned meaning of a,

e denotes a number 1, 2, 3, 4 or 5,

f has the abovementioned meaning of b,

g denotes a number 0 or 1,

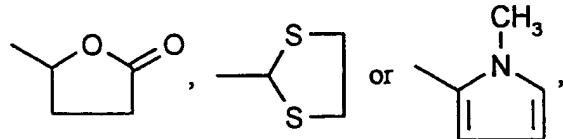
X denotes a 5-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the series comprising N, S and/or O, which is optionally monosubstituted to trisubstituted by nitro, methyl or ethyl.

20

or

X denotes a residue of the formula

25



30

35

or

III. :

40

R^1 , A and T have the abovementioned meaning described in part I or

A represents methyl,

45 R^2 and R^3 have the abovementioned meaning described in part II,

and in this case

50

R^4 represents a 5 to 7 membered, saturated or unsaturated heterocycle, which can contain up to three oxygen, sulphur and/or nitrogen atoms as heteroatoms and to which further a benzene ring can be fused and wherein both rings are optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, halogen, nitro, 1H-tetrazolyl, trifluoromethyl, trifluoromethoxy, difluoromethyl, difluoromethoxy, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 8 carbon atoms or by a group of formula $-\text{NR}^{38}\text{R}^{39}$, $-\text{SR}^{40}$, SO_2R^{41} or $-\text{O-SO}_2\text{R}^{42}$,
in which

55 R^{38} and R^{39} have the meaning shown above for R^{28} and R^{29} and are identical to the latter or different from the latter,

R^{40} has the abovementioned meaning of R^{30} ,

R^{41} and R^{42} are identical or different and have the abovementioned meaning of R^{31} and R^{32} ,

and salts thereof.

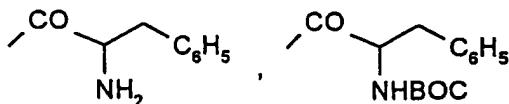
2. Amino-benzofuryl- and thienyl-derivatives of the formula according to claim 1,
wherein

I. :

5

R^1 represents hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms or represents fluorine, chlorine, bromine, nitro, trifluoromethyl or a group of a formula $-OR^5$, $-SR^6$ or $-NR^7R^8$,
in which
10 R^7 denotes hydrogen or a straight-chain or branched alkyl having up to 3 carbon atoms,
 R^5 , R^6 and R^8 are identical or different and denote hydrogen, cyclopropyl, cyclopentyl, cyclohexyl, chinolyl, pyridyl, imidazolyl, 1,3-thiazolyl or thienyl, which are optionally substituted by identical or different substituents from the series comprising fluorine, chlorine, bromine, iodine, cyano, nitro or by a straight-chain or branched alkyl having up to 5 carbon atoms, or
15 denote straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms, or denote phenyl, which is optionally monosubstituted to disubstituted by identical or different substituents from the series comprising nitro, fluorine, chlorine, bromine, iodine, carboxy or straight-chain or branched alkoxy carbonyl having up to 5 carbon atoms,
or
20 R^5 denotes benzyl, acetyl or tetrahydropyranyl.
 R^2 represents formyl or straight-chain or branched acyl, alkoxy or alkoxy carbonyl each having up to 6 carbon atoms in the alkyl group, or represents benzoyl, which is optionally monosubstituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, carboxy, straight-chain or branched alkoxy, alkoxy carbonyl or acyl each having up to 4 carbon atoms
25 in the alkyl group,
or represents a group of a formula

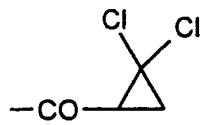
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$-SO_2R^9$, $-CO-(CH_2)_aNR^{10}R^{11}$, $-CO-(CH_2)_bR^{12}$, $-CO-S-R^{13}$ or a residue of the formula

40



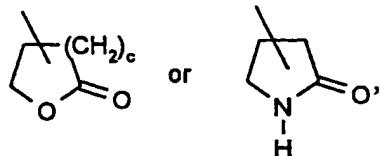
45

R^9 in which
denotes straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally substituted by phenyl, or
denotes phenyl, which is optionally substituted by trifluoromethyl, cyano, nitro or straight-chain or branched alkyl having up to 4 carbon atoms,
50 R^{10} and R^{11} are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 4 carbon atoms or phenyl,
 R^{12} denotes straight-chain or branched alkoxy carbonyl having up to 4 carbon atoms or carboxy,
 a denotes a number 0, 1, 2 or 3,
 b denotes a number 1, 2 or 3,
55 R^{13} denotes straight-chain or branched alkyl having up to 4 carbon atoms,
 R^3 represents hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms, or has the abovementioned meaning of R^2 ,
 T represents an oxygen atom

5 A represents hydrogen, hydroxyl, cyclopropyl, cyclobutyl, cyclopentyl, carboxyl or straight-chain
or a branched alkoxy carbonyl or alkoxyl each having up to 4 carbon atoms, or straight-chain
or branched alkyl or alkenyl each having up to 6 carbon atoms and each of which is optionally
monosubstituted by cyano, tetrazolyl, oxazolyl, oxazolinyl, thiazolyl or a group of a formula

5

10



in which

15 C denotes a number 1 or 2
and in which all rings are optionally monosubstituted by hydroxy, fluorine, bromine, chlorine
or by straight-chain or branched alkyl having up to 4 carbon atoms,
or alkyl or alkenyl are optionally monosubstituted by a group of a formula -CO-R¹⁴, -CO-

20 R¹⁴ in which
denotes hydroxyl, cyclopropyloxy, cyclopentyloxy, cyclohexyloxy or straight-chain or
branched alkyl or alkoxyl each having up to 6 carbon atoms,

R¹⁵ and R¹⁶ are identical or different and represent hydrogen, straight-chain or branched alkyl having up
to 4 carbon atoms, phenyl or benzyl,

25 R¹⁵ or
denotes hydrogen,
and

R¹⁶ denotes hydroxyl,
or

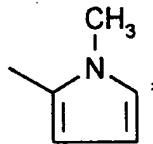
30 R¹⁵ and R¹⁶ R¹⁵ and R¹⁶ together with the nitrogen atom form a pyrrolidinyl, morpholinyl or a piperidinyl ring,
R²¹ represents hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms,
and

R⁴ represents phenyl, which is optionally monosubstituted to trisubstituted by identical or differ-
ent substituents from the series comprising hydroxyl, adamantyl, phenoxy, cyclopropyl,
cyclopentyl, cyclohexyl, fluorine, chlorine, bromine, iodine, nitro, tetrazolyl, furanyl, thienyl,
pyridyl, trifluoromethyl, difluoromethyl, cyano, carboxy, straight-chain or branched alkyl,
alkoxy, alkoxy carbonyl or acyl each having up to 10 carbon atoms in the alkyl group, or
by phenyl, which is optionally monosubstituted to trisubstituted by fluorine, chlorine, bro-
mine, nitro, formyl or straight-chain or branched alkoxy, acyl, ethoxycarbonyl or alkyl each
having up to 4 carbon atoms, which is optionally substituted by hydroxyl, or
phenyl is substituted by a group of formula -NR²⁸R²⁹, -SR³⁰, -SO₂R³¹, -O-SO₂R³² or

35

40

45 R²⁸ in which
N have the meaning shown above for R¹⁰ and R¹¹,
CH₃



50 R²⁸ and R²⁹ in which
R²⁸ have the meaning shown above for R¹⁰ and R¹¹,

or
denotes hydrogen,
and

55 R²⁹ denotes straight-chain or branched acyl having up to 6 carbon atoms,
R³⁰ denotes straight-chain or branched alkyl having up to 4 carbon atoms,
R³¹ and R³² are identical or different and represent straight-chain or branched alkyl having up to 5 carbon
atoms or phenyl, which is optionally substituted by trifluoromethyl, fluorine, chlorine, bromine

or straight-chain or branched alkyl having up to 3 carbon atoms,

with the proviso that A does not denote methyl,

or

II.:

if A represents a methyl group

R¹, T and R⁴ have the abovementioned meaning described in part I,

and in this case

R² and R³ are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms, or

represent formyl or straight-chain or branched acyl, or alkoxycarbonyl each having up to 4 carbon atoms,

or represent benzoyl, which is optionally substituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, carboxy, straight-chain or branched alkoxy, alkoxycarbonyl or acyl each having up to 4 carbon atoms,

or represent a group of a formula -SO₂-(NH)₉-R³³, SO₂NH₂, -CO-(CH₂)_d-NR³⁴R³⁵, -(CH₂)_e-CO-R³⁶, -CO-(CH₂)_f-R³⁷ or CO-X,

in which

R³³ has the abovementioned meaning of R⁹ and is identical or different to the latter,

R³⁴ and R³⁵ are identical or different and denote hydrogen or methyl,

R³⁶ denotes hydroxyl or straight-chain or branched alkoxy having up to 4 carbon atoms or carboxy,

R³⁷ has the abovementioned meaning of R¹² or denotes hydroxyl or straight-chain or branched alkoxy or oxacyl each having up to 4 carbon atoms,

d has the abovementioned meaning of a,

e denotes a number 1, 2, 3 or 4,

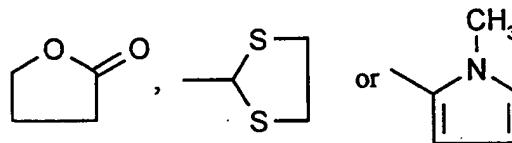
f has the abovementioned meaning of c,

g denotes a number 0 or 1,

X denotes pyrrolyl, furyl or isoxazolyl, which are optionally monosubstituted to trisubstituted by nitro, methyl or ethyl

or

X denotes a residue of the formula



45

or

III.:

R¹, A and T have the meaning described in part I,

or

A represents methyl,

R² and R³ have the meaning described in part II and in this case

R⁴ represents pyridyl, imidazolyl, pyrazolyl, thietyl, isothiazolyl, 1,3-thiazolyl or benzo[b]thiophenyl, where all rings are optionally monosubstituted to trisubstituted by identical or different sub-

stituents from the series comprising hydroxyl, fluorine, chlorine, bromine, iodine, nitro, 1H-tetrazolyl, trifluoromethyl, trifluoromethoxy, difluoromethyl, difluoromethoxy, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 6 carbon atoms or by a group of formula -NR³⁸R³⁹, -SR⁴⁰, -SO₂R⁴¹ or -O-SO₂R⁴²,

in which

5 R³⁸ and R³⁹ have the meaning shown above for R²⁸ and R²⁹ and are identical to the latter or different from the latter,

R⁴⁰ has the abovementioned meaning of R³⁰,

10 R⁴¹ and R⁴² are identical or different and have the abovementioned meaning of R³¹ and R³²,

and salts thereof.

3. Amino-benzofuryl- and thiienyl-derivatives of formula (I) according to claim 1,
wherein

15 I.:

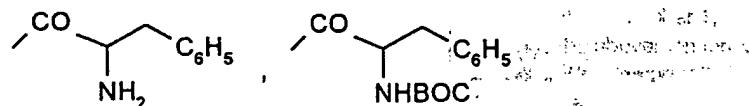
R¹ represents hydrogen, straight-chain or branched alkyl having up to 3 carbon atoms, fluorine, chlorine, bromine, nitro or trifluoromethyl,

20 R² represents formyl or straight-chain or branched acyl, or alkoxy carbonyl each having up to 5 carbon atoms in the alkyl group,

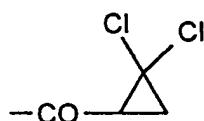
or represents benzoyl, which is optionally substituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, carboxy, straight-chain

25 or branched alkoxy, alkoxy carbonyl or acyl, each having up to 3 carbon atoms in the alkyl group,

or represents a group of a formula



35 -SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO-(CH₂)_b-R¹², -CO-S-R¹³ or a residue of the formula



45 in which

R⁹ denotes straight-chain or branched alkyl having up to 4 carbon atoms, which is optionally substituted by phenyl, or

denotes phenyl, which is optionally substituted by trifluoromethyl, cyano or straight-chain or branched alkyl having up to 3 carbon atoms,

50 R¹⁰ and R¹¹ are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 3 carbon atoms or phenyl,

R¹² denotes straight-chain or branched alkoxy carbonyl having up to 3 carbon atoms or carboxy,

a denotes a number 0, 1, 2 or 3,

b denotes a number 1, 2 or 3,

R¹³ denotes straight-chain or branched alkyl having up to 3 carbon atoms,

55 R³ represents hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms, or has the abovementioned meaning of R²,

T represents an oxygen or sulfur atom,

A represents hydrogen, hydroxyl, cyclopropyl, cyclobutyl, cyclopentyl, carboxyl, or straight-chain

or a branched alkoxy carbonyl or alkoxy each having up to 3 carbon atoms, or straight-chain or branched alkyl having up to 5 carbon atoms which is optionally monosubstituted by cyano or by a group of a formula -CO-R^{14} , $\text{-CO-NR}^{15}\text{R}^{16}$,
in which

- 5 R^{14} denotes hydroxyl, cyclopropoxy, cyclopentyloxy, cyclohexyloxy or straight-chain or branched alkyl or alkoxy having up to 5 carbon atoms,
 R^{15} and R^{16} are identical or different and denote hydrogen, straight-chain or branched alkyl having up to 3 carbon atoms or phenyl,

10 and

- 15 R^4 represents phenyl, which is optionally monosubstituted to trisubstituted by identical or different substituents from the series comprising hydroxyl, adamantyl, phenoxy, N-methyl-pyrrolyl, cyclopropyl, cyclopentyl, cyclohexyl, fluorine, chlorine, bromine, furanyl, thieryl, pyridyl, nitro, trifluoromethyl, difluoromethyl, cyano, carboxyl, methylthio, straight-chain or branched alkyl, alkoxy, acyl or alkoxy carbonyl each having up to 9 carbon atoms, or
 by phenyl, which is optionally monosubstituted to trisubstituted by fluorine, chlorine, bromine, nitro, formyl or straight-chain or branched alkoxy, alkoxy carbonyl, acyl or alkyl each having up to 4 carbon atoms, which is optionally substituted by hydroxyl,

20 with the proviso that A does not denote methyl,
 or
 II.:
 if A represents a methyl group,

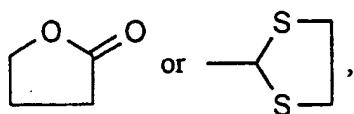
25 R^1 , T and R^4 have the meaning described in part I,

and in this case

- 30 R^2 and R^3 are identical or different and represent hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms, or
 represent formyl or straight-chain or branched acyl or alkoxy carbonyl each having up to 4 carbon atoms,
 or represent benzoyl, which is optionally substituted by substituents from the series comprising fluorine, chlorine, bromine, cyano, straight-chain or branched alkoxy or alkoxy carbonyl each having up to 3 carbon atoms,
 or represent a group of a formula -CO-NH_2 , $\text{-SO}_2\text{(NH)}_9\text{R}^{37}$, $\text{-SO}_2\text{NH}_2$, $\text{-(CH}_2\text{)}_e\text{-CO-R}^{36}$, $\text{-CO-(CH}_2\text{)}_f\text{R}^{37}$ or -CO-X ,
 in which

- 40 R^{33} has the abovementioned meaning of R^9 and is identical or different to the latter,
 R^{34} and R^{35} are identical or different and denote hydrogen or methyl,
 R^{37} has the abovementioned meaning of R^{12} or denotes hydroxyl or straight-chain or branched alkoxy or oxacyl each having up to 4 carbon atoms,
 R^{36} denotes hydroxyl or straight-chain or branched alkoxy having up to 3 carbon atoms,
 d has the abovementioned meaning of a,
 e denotes a number 1, 2, 3 or 4,
 f has the abovementioned meaning of b,
 g denotes a number 0 or 1,
 X denotes pyrrolyl, N-methyl-pyrrolyl, furyl or isoxacolyl, which are optionally monosubstituted to trisubstituted by nitro, methyl or ethyl,
 or
 X denotes a residue of the formula

5



10 b denotes a number 1 or 2,

or

III.:

15 R¹, A and T have the abovementioned meaning described in part I,

or

20 A represents methyl,
R² and R³ have the meaning described in part II,

and in this case

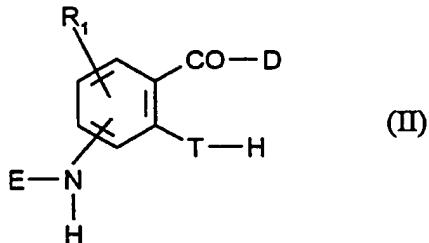
25 R⁴ represents pyridyl, which optionally is up to trisubstituted by identical or different substituents from the series comprising hydroxyl, fluorine, chlorine, bromine, nitro, trifluoromethyl, trifluoromethoxy, difluoromethyl, difluoromethoxy, cyano, carboxy, straight-chain or branched alkyl, alkoxy, alkoxy carbonyl or acyl each having up to 5 carbon atoms,

and salts thereof.

30 4. Amino-benzofuryl- and thienyl-derivatives according to claim 1 to 3 for therapeutic use.

35 5. A process for the preparation of amino-benzofuryl- and thienyl-derivatives according to claims 1 to 3, characterized in that

[A] compounds of the general formula (II)



50

in which

R¹ and T have the abovementioned meaning,

55 and

E denotes straight-chain or branched acyl having up to 4 carbon atoms, preferably acetyl,

and

D represents $(\text{CH}_2)_2(\text{C}_1\text{-}\text{C}_4)$ -alkoxycarbonyl,

5 by reaction with compounds of the formula (III)



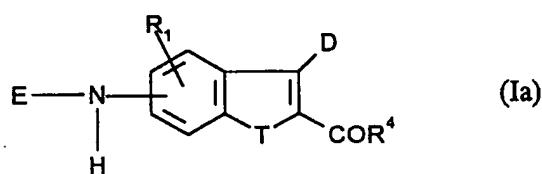
in which

10 R⁴ has the abovementioned meaning

and

15 L represents a leaving group such as chlorine, bromine, tosylate or mesylate,

in inert solvents in the presence of a base,
firstly are converted into compounds of the general formula (Ia)



in which

30 R¹, T, D and E have the abovementioned meaning,

and then the compounds (Ia)
are reacted with compounds of the formula (IV) or (IVa)



40 in which

R² and R³ have the abovementioned meaning,

and

45 L' has the abovementioned meaning of L and is identical or different to the latter,

in inert solvents, if appropriate, in the presence of a base,
and in the case of other radicals mentioned for the meaning of substituent A

50 D is varied, if appropriate, by splitting off protecting groups, alkylation and/or hydrolysis, or

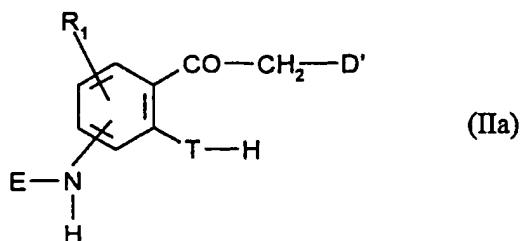
[B] and in the case of A = $\text{CH}_2\text{-CO-R}^{14}$

first compounds of the general formula (IIa)

55

5

10



in which

15

E, T and R¹ have the abovementioned meaning

and

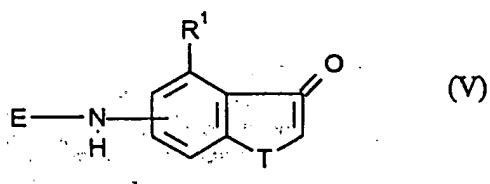
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D' denotes halogen, preferably chlorine,

25

are converted in the presence of NaAc and an alcohol, preferably ethanol, to compounds of the general formula (V)

30



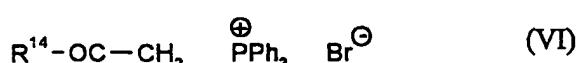
in which

35

R¹, E and T have the abovementioned meaning,

then are reacted with compounds of the general formula (VI)

40



45

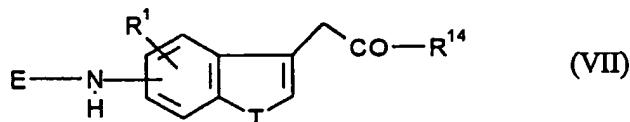
in which

R¹⁴ has the abovementioned meaning

50

to compounds of the general formula (VII)

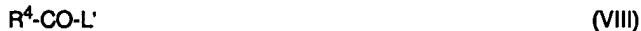
55



in which

E, R¹, T and R¹⁴ have the abovementioned meaning,

5 in inert solvents,
and in a last step are reacted with compounds of the general formula (VIII)



10 in which

R⁴ and L' has the abovementioned meaning,

15 in the presence of 'SnCl₄,

and

optionally followed by reacting with compounds of the general formulae (IV) or (IVa).

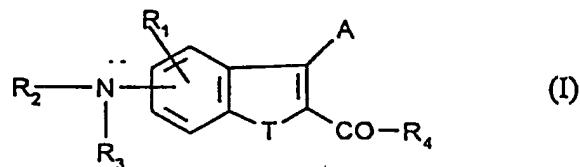
6. A composition consisting of at least one of the amino-benzofuryl- or thiienyl-derivatives according to claim 1 to 3
and a pharmacologically acceptable diluent.
- 20 7. A composition according to claim 6 for the treatment of acute and chronic inflammatory processes.
8. Process for the preparation of compositions according to claim 6 and 7 characterized in that the amino-benzofuryl-
or thiienyl-derivative and the pharmacological acceptable diluent are brought into an formulation suitable for admin-
istration.
- 25 9. Use of amino-benzofuryl- and thiienyl-derivatives according to claim 1 to 3 for the preparation of medicaments.
10. Use according to claim 9 for the preparation of medicaments for the treatment of acute and chronic inflammatory
30 processes.

Patentansprüche

1. Aminobenzofuryl- und -thienylderivate der allgemeinen Formel (I):

35

40



45

worin gilt:

I.:

50 R¹ stellt Wasserstoff oder einen geradkettigen oder verzweigten Alkylrest mit bis zu 4 Kohlenstoffatomen
oder Halogen, eine Carboxyl-, Cyano-, Nitro-, Trifluormethyl- oder eine Gruppe der Formel -OR⁵, -SR⁶
oder -NR⁷R⁸ dar,
worin gilt:

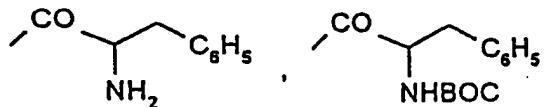
55 R⁵, R⁶ und R⁸ sind gleich oder verschieden und bedeuten Wasserstoff, einen Cycloalkylrest mit 3 bis 6
Kohlenstoffatomen, einen Benzylrest oder einen 5- bis 7-gliedrigen gesättigten oder ungesättigten Hete-
rozyklus mit bis zu 4 Heteroatomen aus den Reihen aus N, S und/oder O, woran ein Phenylring konden-
siert sein kann, und welcher gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den

Reihen aus Halogen, einer Cyano- und aus einer Nitrogruppe oder mit einem geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen substituiert ist, oder
 5 einen geradkettigen oder verzweigten Alkyl- oder Alkenylrest mit jeweils bis zu 8 Kohlenstoffatomen oder einen Phenylrest, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Nitrogruppe, Halogen, einer Carboxygruppe oder aus einem geradkettigen oder verzweigten Alkoxy-carbonylrest mit bis zu 6 Kohlenstoffatomen mono- bis disubstituiert ist,
 oder

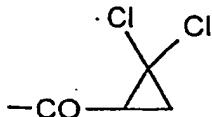
10 R⁵ bedeutet eine Hydroxy-Schutzgruppe aus den Reihen aus: Trimethylsilyl, t-Butyldimethylsilyl, Benzyl, 4-Nitrobenzyl, 4-Methoxybenzyl, Acetyl, Tetrahydropyranyl und aus Benzoyl,

15 R⁷ bedeutet Wasserstoff oder einen geradkettigen oder verzweigten Alkylrest mit bis zu 4 Kohlenstoffatomen,

20 R² stellt eine Formylgruppe oder einen geradkettigen oder verzweigten Acyl-, Alkoxy- oder einen Alkoxy-carbonylrest mit jeweils bis zu 8 Kohlenstoffatomen in der Alkylgruppe oder einen Benzoylrest, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus Halogen, einem Cyano-, Carboxy-, geradkettigem oder verzweigten Alkoxy-, Alkoxy carbonyl- oder aus einem Acylrest mit jeweils bis zu 6 Kohlenstoffatomen in der Alkylgruppe mono- bis trisubstituiert ist,
 oder eine Gruppe der Formeln:



30 -SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO-(CH₂)_bR¹², -CO-S-R¹³
 oder einen Rest der Formel:



40 dar, worin gilt:

45 R⁹ bedeutet einen geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen, der gegebenenfalls mit einem Phenylrest substituiert ist, oder einen Phenylrest, der gegebenenfalls mit einer Trifluormethyl-, Cyano-, Nitrogruppe oder mit einem geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen substituiert ist,

50 R¹⁰ und R¹¹ sind gleich oder verschieden und bedeuten Wasserstoff, einen geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen oder einen Phenylrest,

55 R¹² bedeutet einen geradkettigen oder verzweigten Hydroxyl-, Oxyacyl-, Alkoxy- oder einen Alkoxy carbonylrest mit jeweils bis zu 6 Kohlenstoffatomen oder eine Carboxygruppe,

a bedeutet die Zahl 0, 1, 2 oder 3,

55 b bedeutet die Zahl 1, 2 oder 3,

R¹³ bedeutet einen geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen,

R³ stellt Wasserstoff oder einen geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen

dar oder hat die oben angegebene Bedeutung von R²,

T stellt ein Sauerstoff- oder Schwefelatom dar,

A stellt Wasserstoff, eine Hydroxylgruppe, einen Cycloalkyrest mit 3 bis 6 Kohlenstoffatomen, eine Carboxy- oder geradkettige oder verzweigte Alkoxy carbonyl- oder Alkoxygruppe mit jeweils bis zu 6 Kohlenstoffatomen oder einen geradkettigen oder verzweigten Alkyl- oder Alkenylrest mit jeweils bis zu 8 Kohlenstoffatomen dar, der jeweils gegebenenfalls mit einer Cyanogruppe oder mit einem 5- bis 7-gliedrigen gesättigten oder ungesättigten Heterozyklus mit bis zu 4 Heteroatomen aus den Reihen aus N, S und O monosubstituiert ist, welcher wiederum gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Hydroxygruppe, Halogen, einer Cyano-, Nitro- oder einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 6 Kohlenstoffatomen substituiert ist,

oder die Alkyl- oder Alkenylreste sind gegebenenfalls mit einer Gruppe der Formel substituiert:

15



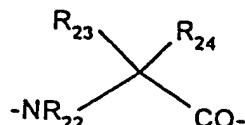
20

worin c die Zahl 1 oder 2 bedeutet,

und worin beide Ringe gegebenenfalls mit einer Hydroxygruppe, Halogen oder einem geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen monosubstituiert ist,

25

oder die Alkyl- oder Alkenylreste sind gegebenenfalls mit einer Gruppe der Formeln -CO-R¹⁴, -CO-NR¹⁵R¹⁶, -CONR¹⁷-SO₂-R¹⁸ oder -PO(OR¹⁹)(OR²⁰), -OR²¹ oder



35

monosubstituiert ist,

worin gilt:

R¹⁴ bedeutet eine Hydroxylgruppe, einen Cycloalkyloxyrest mit 3 bis 7 Kohlenstoffatomen oder eine geradkettige oder verzweigte Alkyl- oder Alkoxygruppe mit jeweils bis zu 8 Kohlenstoffatomen,

40

R¹⁵, R¹⁶ und R¹⁷ sind gleich oder verschieden und stellen Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen, einen Phenyl- oder Benzylrest dar,
oder

45

R¹⁵ bedeutet Wasserstoff,

und

R¹⁶ bedeutet eine Hydroxylgruppe,

oder

50

R¹⁵ und R¹⁶ bilden zusammen mit dem Stickstoffatom einen 5-bis 6-gliedrigen gesättigten Heterozyklus,

R¹⁸ bedeutet eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen, die gegebenenfalls mit einem Phenyl- oder Trifluormethylrest substituiert ist,

55

oder
einen Phenylrest, der gegebenenfalls mit Substituenten aus den Reihen aus Halogen, einer Cyano-, Nitro- oder einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 6 Kohlenstoffatomen substituiert ist,

R¹⁹, R²⁰ und R²¹ sind gleich oder verschieden und stellen Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen dar,

5 R²² bedeutet Wasserstoff, eine Amino-Schutzgruppe oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen,

10 R²³ und R²⁴ sind gleich oder verschieden und bedeuten Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen,
oder

15 R²³ hat die oben angegebene Bedeutung,
und

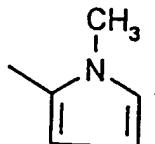
20 R²⁴ bedeutet einen Cycloalkylrest mit 3 bis 6 Kohlenstoffatomen oder einen Arylrest mit 6 bis 10 Kohlenstoffatomen oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 8 Kohlenstoffatomen, die gegebenenfalls mit einer Cyano-, Methylthio-, Hydroxy-, Mercapto-, Guanidyl- oder einer Gruppe der Formel -NR²⁵R²⁶ oder R²⁷-CO- substituiert ist,
worin gilt:

25 R²⁵ und R²⁶ haben die oben für R¹⁵, R¹⁶ und R¹⁷ angegebene Bedeutung.

30 R²⁷ bedeutet eine Hydroxyl-, Benzyloxycarbonyl-, geradkettige oder verzweigte Alkoxygruppe mit bis zu 6 Kohlenstoffatomen oder die oben angegebene Gruppe -NR²⁵R²⁶,

35 oder der Alkylrest ist gegebenenfalls mit einem Cycloalkylrest mit 3 bis 6 Kohlenstoffatomen oder mit einem Arylrest mit 6 bis 10 Kohlenstoffatomen substituiert, welcher gegebenenfalls mit einer Hydroxygruppe, Halogen, einer Nitro-, geradkettigen oder verzweigten Alkoxygruppe mit bis zu 8 Kohlenstoffatomen oder mit der oben angegebenen Gruppe der Formel -NR²⁵R²⁶ substituiert ist,
oder der Alkylrest ist gegebenenfalls mit einem Indolylrest oder mit einem 5- bis 6-gliedrigen ungesättigten Heterozyklus mit bis zu 4 N-Atomen substituiert, worin gegebenenfalls alle -NH-Funktionen mit einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 6 Kohlenstoffatomen oder mit einer Amino-Schutzgruppe geschützt sind,
und

40 R⁴ stellt einen Phenylrest dar, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einem Hydroxyl-, Adamantyl-, Phenoxy-, Cycloalkylrest mit 3 bis 6 Kohlenstoffatomen, aus Halogen, einer Nitro-, Furanyl-, Thieryl-, Pyridyl-, Tetrazolyl-, Trifluormethyl-, Difluormethyl-, Cyano-, Carboxyl-, geradkettigen oder verzweigten Alkyl-, Alkoxy-, Alkoxycarbonyl- oder aus einer Acylgruppe mit jeweils bis zu 11 Kohlenstoffatomen in der Alkylgruppe oder mit einem Phenylrest mono- bis trisubstituiert ist, welcher gegebenenfalls mit einer Nitrogruppe, Halogen, einer Formyl-, Carbonyl- oder einer geradkettigen oder verzweigten Alkoxy-, Acyl-, Alkoxycarbonyl- oder einer Alkylgruppe mit jeweils bis zu 6 Kohlenstoffatomen mono- bis trisubstituiert ist, welche gegebenenfalls mit einer Hydroxylgruppe substituiert ist,
oder der Phenylrest ist mit einer Gruppe der Formeln -NR²⁸R²⁹, -SR³⁰, -SO₂R³¹, -O-SO₂R³²
oder



50 substituiert,
worin gilt:

55 R²⁸ und R²⁹ haben die oben für R¹⁰ und R¹¹ angegebene Bedeutung,
oder

R²⁸ bedeutet Wasserstoff,

und

R²⁹ bedeutet einen geradkettigen oder verzweigten Acylrest mit bis zu 6 Kohlenstoffatomen

5 R³⁰ bedeutet einen geradkettigen oder verzweigten Alkylrest mit bis zu 6 Kohlenstoffatomen,

10 R³¹ und R³² sind gleich oder verschieden und stellen eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen, einen Benzyl- oder Phenylrest dar, die gegebenenfalls mit einer Trifluormethylgruppe, Halogen oder mit einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 6 Kohlenstoffatomen substituiert sind,
mit der Maßgabe, daß A keine Methylgruppe bedeutet,
oder

II.:

15 falls A eine Methylgruppe darstellt,

h

aben R¹, T und R⁴ die in Teil I beschriebene Bedeutung

und in diesem Fall gilt:

20 R² und R³ sind gleich oder verschieden und stellen Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen oder
eine Formyl- oder geradkettige oder verzweigte Acyl-, Alkoxy- oder eine Alkoxycarbonylgruppe mit jeweils bis zu 8 Kohlenstoffatomen,
oder einem Benzoylrest, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen
aus Halogen, einer Cyano-, Carboxy-, geradkettigen oder verzweigten Alkoxy-, Alkoxycarbonyl- oder aus einer
25 Acylgruppe mit jeweils bis zu 6 Kohlenstoffatomen
oder eine Gruppe der Formeln -SO₂(NH)_gR³³, -SO₂NH₂, -CO-(CH₂)_dNR³⁴R³⁵, -(CH₂)_e-CO-R³⁶, -CO-(CH₂)_f-R³⁷ oder -CO-X dar,
worin gilt:

30 R³³ hat die oben angegebene Bedeutung von R⁹ und ist identisch damit oder verschieden davon,

R³⁴ und R³⁵ sind gleich oder verschieden und haben die oben angegebene Bedeutung von R¹⁰ und R¹¹,

35 R³⁶ bedeutet eine Hydroxyl- oder eine geradkettige oder verzweigte Alkoxygruppe mit bis zu 6 Kohlenstoffatomen,

40 R³⁷ hat die oben angegebene Bedeutung von R¹² oder bedeutet eine geradkettige oder verzweigte Alkoxy- oder Oxyacylgruppe mit jeweils bis zu 6 Kohlenstoffatomen oder eine Hydroxylgruppe,
d hat die oben angegebene Bedeutung von a,

e bedeutet die Zahl 1, 2, 3, 4 oder 5,

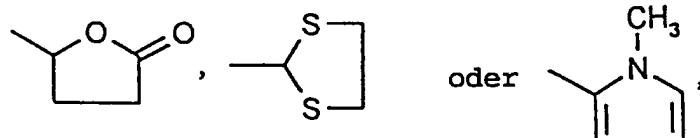
f hat die oben angegebene Bedeutung von b,

g bedeutet die Zahl 0 oder 1,

45 X bedeutet einen 5-gliedrigen gesättigten oder ungesättigten Heterozyklus mit bis zu 3 Heteroatomen aus den Reihen aus N, S und/oder O, der gegebenenfalls mit einer Nitro-, Methyl- oder einer Ethylgruppe mono- bis trisubstituiert ist, oder

X bedeutet einen Rest der Formeln:

50



55

oder

III.:

R¹, A und T haben die in Teil I beschriebene Bedeutung,

oder

A stellt eine Methylgruppe dar,

R² und R³ haben die in Teil II beschriebene Bedeutung,

und in diesem Fall gilt:

R⁴ stellt einen 5- bis 7-gliedrigen gesättigten oder ungesättigten Heterozyklus dar, der bis zu 3 Sauerstoff-, Schwefel- und/oder Stickstoffatome als Heteroatome enthalten kann, woran ferner ein Benzolring kondensiert sein kann, und worin beide Ringe gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Hydroxylgruppe, Halogen, einer Nitro-, 1H-Tetrazolyl-, Trifluormethyl-, Trifluormethoxy-, Difluormethyl-, Difluormethoxy-, Cyano-, Carboxy-, geradkettigen oder verzweigten Alkyl-, Alkoxy-, Alkoxycarbonyl- oder aus einer Acylgruppe mit jeweils bis zu 8 Kohlenstoffatomen oder mit einer Gruppe der Formeln -NR³⁸R³⁹, -SR⁴⁰, -SO₂R⁴¹ oder -O-SO₂R⁴² mono- bis trisubstituiert sind,
worin gilt:

R³⁸ und R³⁹ haben die oben für R²⁸ und R²⁹ angegebene Bedeutung und sind mit den letzteren identisch oder davon verschieden,

R⁴⁰ hat die oben angegebene Bedeutung von R³⁰,

R⁴¹ und R⁴² sind gleich oder verschieden und haben die oben angegebene Bedeutung von R³¹ und R³², und Salze davon.

2. Aminobenzofuryl- und -thienylderivate der Formel gemäß Anspruch 1,
worin gilt:

I.:

R¹ stellt Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen oder Fluor, Chlor, Brom, eine Nitro-, Tri-fluormethyl- oder eine Gruppe der Formeln -OR⁵, -SR⁶ oder -NR⁷R⁸ dar,
worin gilt:

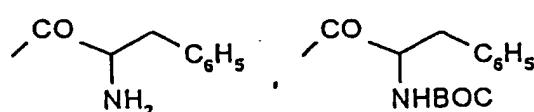
R⁷ bedeutet Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen, R⁵, R⁶ und R⁸ sind gleich oder verschieden und bedeuten Wasserstoff, Cyclopropyl, Cyclopentyl, Cyclohexyl, Chinolyl, Pyridyl, Imidazolyl, 1,3-Thiazolyl oder Thienyl, welche gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus Fluor, Chlor, Brom, Jod, einer Cyano- und aus einer Nitrogruppe oder

mit einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 5 Kohlenstoffatomen substituiert sind, oder eine geradkettige oder verzweigte Alkyl- oder Alkenylgruppe mit jeweils bis zu 6 Kohlenstoffatomen oder einen Phenylrest, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Nitrogruppe, Fluor, Chlor, Brom, Jod, einer Carboxy- oder aus einer geradkettigen oder verzweigten Alkoxycarbonylgruppe mit bis zu 5 Kohlenstoffatomen mono- bis disubstituiert ist,
oder

R⁵ bedeutet eine Benzyl-, Acetyl- oder eine Tetrahydropyranylgruppe,

R² stellt eine Formylgruppe oder eine geradkettige oder verzweigte Acyl-, Alkoxy- oder Alkoxycarbonylgruppe mit jeweils bis zu 6 Kohlenstoffatomen in der Alkylgruppe

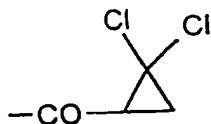
oder eine Benzoylgruppe, die gegebenenfalls mit Substituenten aus der Reihe aus Fluor, Chlor, Brom, einer Cyano-, Carboxy-, geradkettigen oder verzweigten Alkoxy-, Alkoxycarbonyl- oder einer Acylgruppe mit jeweils bis zu 4 Kohlenstoffatomen in der Alkylgruppe monosubstituiert ist,
oder eine Gruppe der Formeln:



55 -SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹,

-CO-(CH₂)_bR¹², -CO-S-R¹³ oder einen Rest der Formel

5



dar,

10

worin gilt:

R^9 bedeutet eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen, die gegebenenfalls mit einem Phenylrest substituiert ist, oder
einen Phenylrest, der gegebenenfalls mit einer Trifluormethyl-, Cyano-, Nitro- oder mit einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 4 Kohlenstoffatomen substituiert ist,

15

R^{10} und R^{11} sind gleich oder verschieden und bedeuten Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen oder einen Phenylrest,
 R^{12} bedeutet eine geradkettige oder verzweigte Alkoxy carbonylgruppe mit bis zu 4 Kohlenstoffatomen oder eine Carboxygruppe,

20

a bedeutet die Zahl 0, 1, 2 oder 3,

b bedeutet die Zahl 1, 2 oder 3,

 R^{13} bedeutet eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen,

R^3 stellt Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen dar
oder hat die oben angegebene Bedeutung von R^2 ,

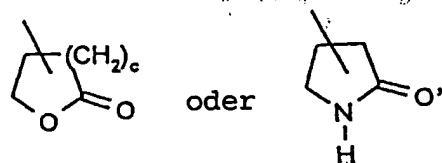
T stellt ein Sauerstoffatom dar,

25

A stellt Wasserstoff, eine Hydroxyl-, Cyclopropyl-, Cyclobutyl-, Cyclopentyl-, Carboxyl- oder eine geradkettige oder verzweigte Alkoxy carbonyl- oder Alkoxygruppe mit jeweils bis zu 4 Kohlenstoffatomen oder eine geradkettige oder verzweigte Alkyl- oder Alkenylgruppe mit jeweils bis zu 6 Kohlenstoffatomen dar, die jeweils gegebenenfalls mit einer Cyano-, Tetrazolyl-, Oxazolyl-, Oxazolinyl-, Thiazolyl- oder mit einer Gruppe der Formel

30

35



monosubstituiert ist,

40

worin gilt:

c bedeutet die Zahl 1 oder 2,

und worin alle Ringe gegebenenfalls mit einer Hydroxygruppe, Fluor, Brom, Chlor oder mit einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 4 Kohlenstoffatomen monosubstituiert sind,

45

oder die Alkyl- oder Alkenylgruppen sind gegebenenfalls mit einer Gruppe der Formeln $-CO-R^{14}$, $-CO-NR^{15}R^{16}$ oder $-OR^{21}$ monosubstituiert,

worin gilt:

R^{14} bedeutet eine Hydroxyl-, Cyclopropoxy-, Cyclopentyloxy-, Cyclohexyloxy- oder eine geradkettige oder verzweigte Alkyl- oder Alkoxygruppe mit jeweils bis zu 6 Kohlenstoffatomen,

50

R^{15} und R^{16} sind gleich oder verschieden und stellen Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen, einen Phenyl- oder Benzylrest dar,

oder

 R^{15} bedeutet Wasserstoff, und R^{16} bedeutet eine Hydroxylgruppe,

oder

R^{15} und R^{16} bilden zusammen mit dem Stickstoffatom einen Pyrrolidinyl-, Morpholinyl- oder einen Piperidinylring,

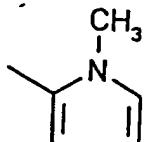
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R^{21} stellt Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 6 Kohlenstoffatomen dar,
und

5 R⁴ stellt einen Phenylrest dar, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus Hydroxyl, Adamantyl, Phenoxy, Cyclopropyl, Cyclopentyl, Cyclohexyl, Fluor, Chlor, Brom, Jod, einer Nitro-, Tetrazolyl-, Furanyl-, Thienyl-, Pyridyl-, Trifluormethyl-, Difluormethyl-, Cyano-, Carboxy-, einer geradkettigen oder verzweigten Alkyl-, Alkoxy-, Alkoxy carbonyl- oder aus einer Acylgruppe mit jeweils bis zu 10 Kohlenstoffatomen in der Alkylgruppe oder

10 mit einem Phenylrest mono- bis trisubstituiert ist, der gegebenenfalls mit Fluor, Chlor, Brom, einer Nitro-, Formyl- oder einer geradkettigen oder verzweigten Alkoxy-, Acyl-, Ethoxycarbonyl- oder mit einer Alkylgruppe mit jeweils bis zu 4 Kohlenstoffatomen mono- bis trisubstituiert ist, die gegebenenfalls mit einer Hydroxylgruppe substituiert ist, oder

10 der Phenylrest ist mit einer Gruppe der Formeln -NR²⁸R²⁹, -SR³⁰, -SO₂R³¹, -O-SO₂R³² oder

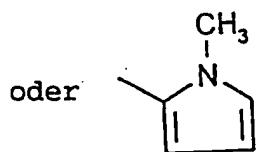
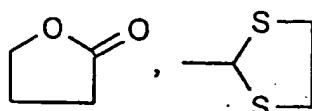


20 substituiert,
 worin gilt:
 R²⁸ und R²⁹ haben die oben für R¹⁰ und R¹¹ angegebene Bedeutung,
 oder
 R²⁸ bedeutet Wasserstoff,
25 und
 R²⁹ bedeutet eine geradkettige oder verzweigte Acylgruppe mit bis zu 6 Kohlenstoffatomen,
 R³⁰ bedeutet eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen,
 R³¹ und R³² sind gleich oder verschieden und stellen eine geradkettige oder verzweigte Alkylgruppe mit bis zu 5 Kohlenstoffatomen oder einen Phenylrest dar, der gegebenenfalls mit einer Trifluormethylgruppe, Fluor, Chlor, Brom oder mit einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 3 Kohlenstoffatomen substituiert ist,
30 mit der Maßgabe, daß A keine Methylgruppe bedeutet,
 oder
 II.:
35 falls A eine Methylgruppe darstellt,
 haben R¹, T und R⁴ die in Teil I beschriebene Bedeutung und in diesem Fall gilt:
 R² und R³ sind gleich oder verschieden und stellen Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen oder
 eine Formyl- oder geradkettige oder verzweigte Acyl- oder Alkoxy carbonylgruppe mit jeweils bis zu 4 Kohlenstoffatomen
40 oder eine Benzoylgruppe, die gegebenenfalls mit Substituenten aus den Reihen aus Fluor, Chlor, Brom, einer Cyano-, Carboxy-, einer geradkettigen oder verzweigten Alkoxy-, Alkoxy carbonyl- oder aus einer Acylgruppe mit jeweils bis zu 4 Kohlenstoffatomen substituiert ist,
 oder eine Gruppe der Formel -SO₂-(NH)₉-R³³, -SO₂NH₂, -CO-(CH₂)_d-NR³⁴R³⁵, -(CH₂)_e-CO-R³⁶, -CO-(CH₂)_f-R³⁷ oder -CO-X dar,
45 worin gilt:
 R³³ hat die oben angegebene Bedeutung von R⁹ und ist gleich damit oder verschieden davon,
 R³⁴ und R³⁵ sind gleich oder verschieden und bedeuten Wasserstoff oder eine Methylgruppe,
 R³⁶ bedeutet eine Hydroxylgruppe oder eine geradkettige oder verzweigte Alkoxygruppe mit bis zu 4 Kohlenstoffatomen oder eine Carboxygruppe,
50 R³⁷ hat die oben angegebene Bedeutung von R¹² oder bedeutet eine Hydroxylgruppe oder eine geradkettige oder verzweigte Alkoxygruppe oder eine Oxacylgruppe mit jeweils bis zu 4 Kohlenstoffatomen,
 d hat die oben angegebene Bedeutung von a,
 e bedeutet die Zahl 1, 2, 3 oder 4,
55 f hat die oben angegebene Bedeutung von c,
 g bedeutet die Zahl 0 oder 1,
 X bedeutet Pyrrolyl, Furyl oder Isoxazolyl, welche gegebenenfalls mit einer Nitro-, Methyl- oder mit einer Ethylgruppe mono- bis trisubstituiert sind,

oder

X bedeutet einen Rest der Formeln:

5



10

oder

III.:

- 15 R¹, A und T haben die in Teil I beschriebene Bedeutung, oder
A stellt eine Methylgruppe dar,
R² und R³ haben die oben angegebene Bedeutung, die in Teil II beschrieben ist,
und in diesem Fall gilt:
20 R⁴ stellt Pyridyl, Imidazolyl, Pyrazolyl, Thienyl, Isothiazolyl, 1,3-Thiazolyl oder Benzo[b]thiophenyl dar, worin alle Ringe gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Hydroxylgruppe, Fluor, Chlor, Brom, Jod, einer Nitro-, 1H-Tetrazolyl-, Trifluormethyl-, Trifluormethoxy-, Difluormethyl-, Difluormethoxy-, Cyano-, Carboxy-, einer geradkettigen oder verzweigten Alkyl-, Alkoxy-, Alkoxy carbonyl- oder aus einer Acylgruppe mit jeweils bis zu 6 Kohlenstoffatomen oder mit einer Gruppe der Formeln -NR³⁸R³⁹, -SR⁴⁰, -SO₂R⁴¹ oder -O-SO₂R⁴² mono- bis trisubstituiert sind,
25 worin gilt:
R³⁸ und R³⁹ haben die oben für R²⁸ und R²⁹ angegebene Bedeutung und sind identisch damit oder verschieden davon,
R⁴⁰ hat die oben angegebene Bedeutung von R³⁰,
R⁴¹ und R⁴² sind gleich oder verschieden und haben die oben angegebene Bedeutung von R³¹ und R³²,
30 und Salze davon.

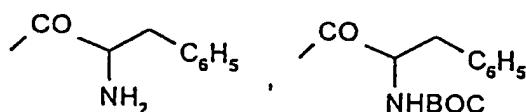
3. Aminobenzofuryl- und -thienylderivate der Formel (I) gemäß Anspruch 1,
worin gilt:

35

I.:

- R¹ stellt Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen, Fluor, Chlor, Brom, einen Nitro- oder Trifluormethylgruppe dar.
R² stellt eine Formylgruppe oder eine geradkettige oder verzweigte Acylgruppe oder eine Alkoxy carbonylgruppe mit jeweils bis zu 5 Kohlenstoffatomen in der Alkylgruppe
40 oder eine Benzoylgruppe, die gegebenenfalls mit Substituenten aus den Reihen aus Fluor, Chlor, Brom, einer Cyano-, Carboxy-, einer geradkettigen oder verzweigten Alkoxy-, Alkoxy carbonyl- oder aus einer Acylgruppe mit jeweils bis zu 3 Kohlenstoffatomen in der Alkylgruppe substituiert ist,
oder eine Gruppe der Formeln:

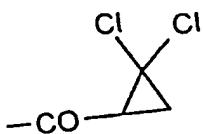
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50

-SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹,
-CO-(CH₂)_b-R¹², -CO-S-R¹³ oder einen Rest der Formel

55



- 10 dar,
worin gilt:
R⁹ bedeutet eine geradkettige oder verzweigte Alkylgruppe mit bis zu 4 Kohlenstoffatomen, die gegebenenfalls mit einem Phenylrest substituiert ist, oder
einen Phenylrest, der gegebenenfalls mit einer Trifluormethyl-, Cyano- oder einer geradkettigen oder verzweigten Alkylgruppe mit bis zu 3 Kohlenstoffatomen substituiert ist,
R¹⁰ und R¹¹ sind gleich oder verschieden und bedeuten Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen oder einen Phenylrest,
R¹² bedeutet eine geradkettige oder verzweigte Alkoxy carbonylgruppe mit bis zu 3 Kohlenstoffatomen oder eine Carboxygruppe,
20 a bedeutet die Zahl 0, 1, 2 oder 3,
b bedeutet die Zahl 1, 2 oder 3,
R¹³ bedeutet eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen,
R³ stellt Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen dar oder hat die oben angegebene Bedeutung von R²,
25 T stellt ein Sauerstoff- oder Schwefelatom dar,
A stellt Wasserstoff, eine Hydroxyl-, Cyclopropyl-, Cyclobutyl-, Cyclopentyl-, Carboxyl- oder eine geradkettige oder verzweigte Alkoxy carbonyl- oder Alkoxygruppe mit jeweils bis zu 3 Kohlenstoffatomen oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 5 Kohlenstoffatomen dar; die gegebenenfalls mit einer Cyano- oder einer Gruppe der Formeln -CO-R¹⁴, -CO-NR¹⁵R¹⁶ monosubstituiert ist, worin gilt:
30 R¹⁴ bedeutet eine Hydroxyl-, Cyclopropoxy-, Cyclopentyloxy-, Cyclohexyloxy- oder eine geradkettige oder verzweigte Alkyl- oder Alkoxygruppe mit bis zu 5 Kohlenstoffatomen,
R¹⁵ und R¹⁶ sind gleich oder verschieden und bedeuten Wasserstoff, eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen oder einen Phenylrest, und
35 R⁴ stellt einen Phenylrest dar, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Hydroxyl-, Adamantyl-, Phenoxy-, N-Methylpyrrolyl-, Cyclopropyl-, Cyclopentyl-, Cyclohexylgruppe, Fluor, Chlor, Brom, einer Furanyl-, Thienyl-, Pyridyl-, Nitro-, Trifluormethyl-, Difluormethyl-, Cyano-, Carboxyl-, Methylthio-, einer geradkettigen oder verzweigten Alkyl-, Alkoxy-, Acyl- oder aus einer Alkoxy carbonylgruppe mit jeweils bis zu 9 Kohlenstoffatomen
oder
40 mit einem Phenylrest mono- bis trisubstituiert ist, der gegebenenfalls mit Fluor, Chlor, Brom, einer Nitro-, Formyl- oder einer geradkettigen oder verzweigten Alkoxy-, Alkoxy carbonyl-, Acyl- oder mit einer Alkylgruppe mit bis zu 4 Kohlenstoffatomen mono- bis trisubstituiert ist, die gegebenenfalls mit einer Hydroxylgruppe substituiert ist,
45 mit der Maßgabe, daß A keine Methylgruppe bedeutet,
oder
II.:
falls A eine Methylgruppe darstellt,
haben R¹, T und R⁴ die in Teil I beschriebene Bedeutung,
50 und in diesem Fall gilt:
R² und R³ sind gleich oder verschieden und stellen Wasserstoff oder eine geradkettige oder verzweigte Alkylgruppe mit bis zu 3 Kohlenstoffatomen oder
eine Formylgruppe oder eine geradkettige oder verzweigte Acyl- oder Alkoxy carbonylgruppe mit jeweils bis zu 4 Kohlenstoffatomen
55 oder eine Benzoylgruppe, die gegebenenfalls mit Substituenten aus den Reihen aus Fluor, Chlor, Brom, einer Cyano-, geradkettigen oder verzweigten Alkoxy- oder Alkoxy carbonylgruppe mit jeweils bis zu 3 Kohlenstoffatomen substituiert ist,
oder eine Gruppe der Formeln -CO-NH₂, -SO₂(NH)₉R³⁷, -SO₂NH₂, -(CH₂)₆-COR³⁶, -CO-(CH₂)₇R³⁷ oder -

CO-X

dar,

worin gilt:

R³³ hat die oben angegebene Bedeutung von R⁹ und ist identisch damit oder verschieden davon,R³⁴ und R³⁵ sind gleich oder verschieden und bedeuten Wasserstoff oder eine Methylgruppe,R³⁷ hat die oben angegebene Bedeutung von R¹² oder bedeutet eine Hydroxylgruppe oder eine geradkettige oder verzweigte Alkoxy- oder eine Oxacylgruppe mit jeweils bis zu 4 Kohlenstoffatomen,R³⁶ bedeutet eine Hydroxylgruppe oder eine geradkettige oder verzweigte Alkoxygruppe mit bis zu 3 Kohlenstoffatomen,

10 e bedeutet die Zahl 1, 2, 3 oder 4,

f hat die oben angegebene Bedeutung von b,

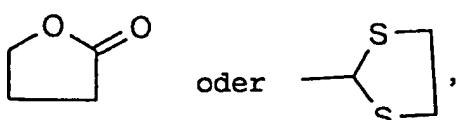
g bedeutet die Zahl 0 oder 1,

X bedeutet Pyrrolyl, N-Methylpyrrolyl, Furyl oder Isoxazolyl, welche gegebenenfalls mit einer Nitro-, Methyl- oder einer Ethylgruppe mono- bis trisubstituiert sind,

15 oder

X bedeutet einen Rest der Formeln:

20



25

b bedeutet die Zahl 1 oder 2,

oder

III.:

R¹, A und T haben die oben angegebene Bedeutung, die in Teil I beschrieben ist,

30 oder

A stellt eine Methylgruppe dar,

wobei

R² und R³ die in Teil II beschriebene Bedeutung haben, und in diesem Fall gilt:35 R⁴ stellt einen Pyridylrest dar, der gegebenenfalls mit gleichen oder verschiedenen Substituenten aus den Reihen aus einer Hydroxylgruppe, Fluor, Chlor, Brom, einer Nitro-, Trifluormethyl-, Trifluormethoxy-, Difluormethyl-, Difluormethoxy-, Cyano-, Carboxy-, einer geradkettigen oder verzweigten Alkyl-, Alkoxy-, Alkoxy carbonyl- oder aus einer Acylgruppe mit jeweils bis zu 5 Kohlenstoffatomen mono- bis trisubstituiert ist, und Salze davon.

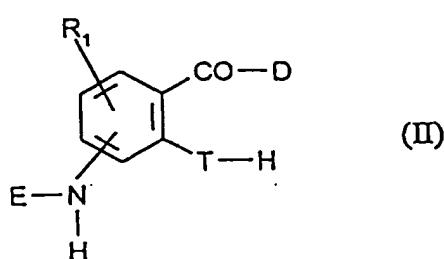
40 4. Aminobenzofuryl- und -thienylderivate gemäß einem der Ansprüche 1 bis 3 zur therapeutischen Verwendung.

5. Verfahren zur Herstellung der Aminobenzofuryl- und -thienyl-derivate gemäß einem der Ansprüche 1 bis 3, dadurch gekennzeichnet, daß

45

[A] Verbindungen der allgemeinen Formel (II):

50



55

worin gilt:

R¹ und T haben die oben angegebene Bedeutung,

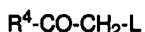
und

E bedeutet eine geradkettige oder verzweigte Acylgruppe mit bis zu 4 Kohlenstoffatomen, vorzugsweise eine Acetylgruppe,

und

D stellt eine -(CH₂)₂-(C₁-C₄)-Alkoxycarbonylgruppe dar,
durch Reaktion mit Verbindungen der Formel (III):

10



(III)

worin gilt:

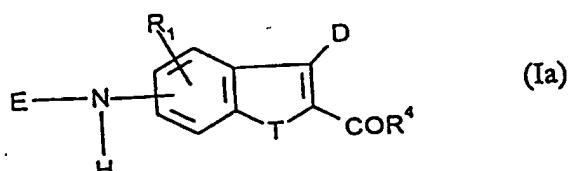
R⁴ hat die oben angegebene Bedeutung,

und

15

L stellt eine Abgangsgruppe dar, wie Chlor, Brom, eine Tosylat- oder Mesylatgruppe,
in inerten Lösungsmitteln in der Gegenwart einer Base zuerst in Verbindungen der allgemeinen Formel (Ia)
überführt werden:

20



25

worin gilt:

30

R¹, T, D und E haben die oben angegebene Bedeutung,
und daß dann die Verbindungen (Ia)
mit Verbindungen der Formeln (IV) oder (IVa):



35



worin gilt:

R² und R³ haben die oben angegebene Bedeutung,

und

40

L' hat die oben angegebene Bedeutung von L und ist identisch damit oder verschieden davon,
in inerten Lösungsmitteln, gegebenenfalls in der Gegenwart einer Base, umgesetzt werden, und daß im Falle
weiterer Reste, die für die Bedeutung von Substituent A angegeben sind,

45

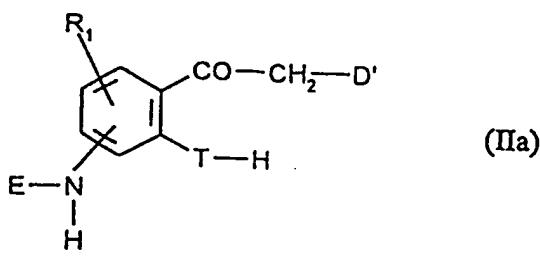
D abgeändert wird, gegebenenfalls durch Abspaltung von Schutzgruppen, Alkylierung und/oder Hydrolyse,
oder daß

[B] im Fall von A = -CH₂-CO-R¹⁴

zuerst Verbindungen der allgemeinen Formel (IIa):

50

55



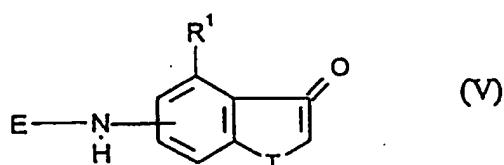
worin gilt:

E, T und R¹ haben die oben angegebene Bedeutung,

und

D' bedeutet Halogen, vorzugsweise Chlor,

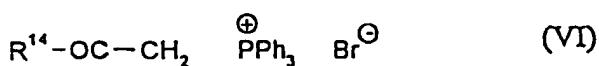
in der Gegenwart von NaAc und einem Alkohol, vorzugsweise von Ethanol, in Verbindungen der allgemeinen Formel (V) überführt werden:



worin gilt:

R¹, E und T haben die oben angegebene Bedeutung,

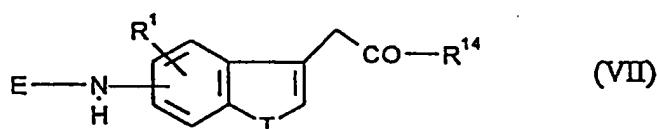
welche dann mit Verbindungen der allgemeinen Formel (VI):



worin

R¹⁴ die oben angegebene Bedeutung hat,

zu Verbindungen der allgemeinen Formel (VII):



50

worin

E, R¹, T und R¹⁴ die oben angegebene Bedeutung haben,

in inerten Lösungsmitteln umgesetzt werden,

welche in einer letzten Stufe mit Verbindungen der allgemeinen Formel (VIII):

55



worin

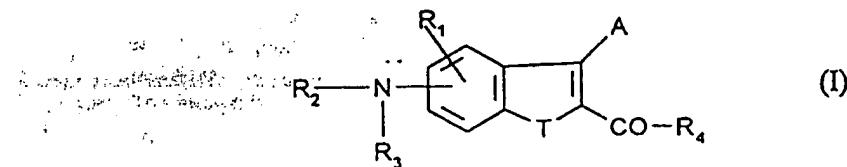
R^4 und L' die oben angegebene Bedeutung haben,
in der Gegenwart von SnCl_4 zur Reaktion gebracht werden, und daß
gegebenenfalls des weiteren eine Reaktion mit Verbindungen der allgemeinen Formeln (IV) oder (IVa) durchgeführt wird.

- 5 6. Zusammensetzung aus mindestens einem der Aminobenzofuryl- oder -thienylderivate gemäß einem der Ansprüche 1 bis 3 und aus einem pharmakologisch geeigneten Verdünnungsmittel.
- 10 7. Zusammensetzung gemäß Anspruch 6 zur Behandlung akuter und chronischer Entzündungen.
- 15 8. Verfahren zur Herstellung von Zusammensetzungen gemäß Anspruch 6 oder 7,
dadurch gekennzeichnet, daß
die Aminobenzofuryl- oder -thienylderivate und das pharmakologisch geeignete Verdünnungsmittel in eine zur Verabreichung geeignete Zubereitung eingebracht werden.
- 20 9. Verwendung der Aminobenzofuryl- und -thienylderivate gemäß einem der Ansprüche 1 bis 3 zur Herstellung von Medikamenten.
- 25 10. Verwendung gemäß Anspruch 9 zur Herstellung von Medikamenten zur Behandlung akuter und chronischer Entzündungen.

Revendications

1. Dérivés d'amino-benzofuryle et -thiényle, de formule générale (I)

25



35 dans laquelle

R^1 représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifiée ayant jusqu'à 6 atomes de carbone ou représente un halogène, un groupe carboxyle, cyano, nitro, trifluorométhyle ou un groupe de formule $-OR^5$, $-SR^6$ ou $-NR^7R^8$,

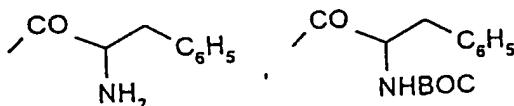
40 dans laquelle
 R^5 , R^6 et R^8 sont identiques ou différents et représentent l'hydrogène, un groupe cycloalkyle ayant 3 à 6 atomes de carbone, un groupe benzyle ou hétérocycle penta- à heptagonal sature ou insaturé ayant jusqu'à 4 hétéroatomes choisis dans le groupe comprenant N, S et/ou O et auquel un noyau phényle peut être condensé et qui est facultativement substitué avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants halogéno, cyano et nitro ou avec un substituant alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, ou représentent un groupe alkyle ou alcényle à chaîne droite ou ramifié ayant chacun jusqu'à 8 atomes de carbone, ou représentent un groupe phényle, qui est facultativement monosubstitué à disubstitué avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants nitro, halogéno, carboxy ou alkoxykarbonyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,

50 ou
 R^5 représente un groupe protecteur de la fonction hydroxyle, choisi entre les groupes triméthylsilyle, tertio-butyldiméthylsilyle, benzyle, 4-nitrobenzyle, 4-méthoxybenzyle, acétyle, tétrahydropyranyle et benzoyle,
 R^7 représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone,

55 R^2 représente un groupe formyle ou un groupe, à chaîne droite ou ramifié, acyle, alkoxy ou alkoxykarbonyle ayant chacun jusqu'à 8 atomes de carbone dans le groupe alkyle, ou représente un groupe benzoyle, qui est facultativement mono-substitué à trisubstitué avec des substituants identiques ou différents choisis dans

le groupe comprenant des substituants halogéno, cyano, carboxy, alkoxy, alkoxycarbonyle ou acyle à chaîne droite ou ramifié, ayant chacun jusqu'à 6 atomes de carbone dans le groupe alkyle, ou représente un groupe de formule

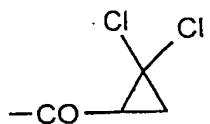
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10

$-\text{SO}_2\text{R}^9$, $-\text{CO}-(\text{CH}_2)_a\text{NR}^{10}\text{R}^{11}$, $-\text{CO}-(\text{CH}_2)_b\text{-R}^{12}$, $-\text{CO-S-R}^{13}$ ou un résidu de formule

15



20

dans lequel

R^9 représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, qui est facultativement substitué avec un substituant phényle, ou représente un groupe phényle, qui est facultativement substitué avec un substituant trifluorométhyle, cyano, nitro ou alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,

25

R^{10} et R^{11} sont identiques ou différents et représentent l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone ou un groupe phényle,

R^{12} représente un groupe, à chaîne droite ou ramifié, hydroxyle, oxyacyle, alloxy ou alkoxycarbonyle ayant chacun jusqu'à 6 atomes de carbone ou un groupe carboxy,

30

a représente le nombre 0, 1, 2 ou 3,

b représente le nombre 1, 2 ou 3,

R^{13} représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,

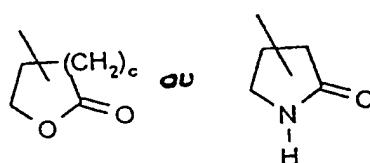
R^3 représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, ou bien répond à la définition précitée de R^2 ,

35

T représente un atome d'oxygène ou de soufre,

A représente l'hydrogène, un groupe hydroxyle, cycloalkyle ayant 3 à 6 atomes de carbone, carboxy ou alkoxycarbonyle ou alkoxy à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone, ou un groupe alkyle ou alcényle à chaîne droite ou ramifié ayant jusqu'à 8 atomes de carbone, chacun étant facultativement mono-substitué avec un substituant cyano ou avec un hétérocycle penta- à heptagonal saturé ou insaturé ayant jusqu'à 4 hétéroatomes du groupe comprenant N, S et O, qui est facultativement substitué avec des substituants identiques ou différents du groupe comprenant des substituants hydroxy, halogéno, cyano, nitro ou avec un substituant alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, ou les groupes alkyle ou alcényle sont facultativement substitués avec un groupe de formule

45



50

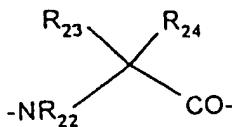
dans laquelle

55

c représente le nombre 1 ou 2,

et dans laquelle les deux noyaux sont facultativement monosubstitués avec un substituant hydroxy ou halogéno ou avec un substituant alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, ou les groupes alkyle ou alcényle sont facultativement monosubstitués avec un groupe de formule $-\text{CO-R}^{14}$,

-CO-NR¹⁵R¹⁶, -CONR¹⁷-SO₂-R¹⁸ ou -PO(OR¹⁹)(OR²⁰), -OR²¹ ou



10

dans laquelle

R¹⁴ représente un groupe hydroxyle, cycloalkyloxy ayant 3 à 7 atomes de carbone ou un groupe alkyle ou alkoxy à chaîne droite ou ramifié ayant chacun jusqu'à 8 atomes de carbone,

15

R¹⁵, R¹⁶ et R¹⁷ sont identiques ou différents et représentent l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, un groupe phényle ou benzyle,

ou

R¹⁵ représente l'hydrogène,

et

R¹⁶ représente un groupe hydroxyle,

20

ou

R¹⁵ et R¹⁶ conjointement avec l'atome d'azote, forment un hétérocycle penta- ou hexagonal saturé,

R¹⁸ représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, qui est facultativement substitué avec un substituant phényle ou trifluorométhyle,

ou

représente un groupe phényle, qui est facultativement substitué avec des substituants faisant partie du groupe comprenant des substituants halogéno, cyano et nitro ou avec un substituant alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,

R¹⁹, R²⁰ et R²¹ sont identiques ou différents et représentent l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,

R²² représente l'hydrogène, un groupe protecteur de la fonction amino ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,

R²³ et R²⁴ sont identiques ou différents et représentent l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone,

ou

R²³ répond à la définition précitée,

et

R²⁴ représente un groupe cycloalkyle ayant 3 à 6 atomes de carbone ou un groupe aryle ayant 6 à 10 atomes de carbone ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 8 atomes de carbone, qui est facultativement substitué avec un substituant cyano, méthylthio, hydroxy, mercapto, guanidyle ou un groupe de formule -NR²⁵R²⁶ ou R²⁷-CO-,

40

dans laquelle

R²⁵ et R²⁶ répondent à la définition mentionnée ci-dessus pour R¹⁵, R¹⁶ et R¹⁷,

R²⁷ représente un groupe hydroxyle, benzyloxycarbonyle, alkoxy à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone ou le groupe -NR²⁵R²⁶ précité,

45

ou le groupe alkyle est facultativement substitué avec un substituant cycloalkyle ayant 3 à 6 atomes de carbone, ou avec un substituant aryle ayant 6 à 10 atomes de carbone, qui est facultativement substitué avec un substituant hydroxyle, halogéno, nitro, alkoxy à chaîne droite ou ramifié ayant jusqu'à 8 atomes de carbone ou avec le groupe précité, de formule -NR²⁵R²⁶,

50

ou le groupe alkyle est facultativement substitué avec un substituant indolyle ou avec un hétérocycle penta- ou hexagonal insaturé ayant jusqu'à 4 atomes de N dans lequel, facultativement, toutes les fonctions -NH sont protégées avec des groupes alkyle à chaîne droite ou ramifiés ayant jusqu'à 6 atomes de carbone ou avec un groupe protecteur de la fonction amino,

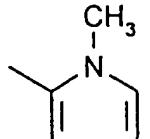
et

55

R⁴ représente un groupe phényle, qui est facultativement monosubstitué à trisubstitué avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants hydroxyle, adamantyle, phenoxy, cycloalkyle ayant 3 à 6 atomes de carbone, halogéno, nitro, furannyle, thiényle, pyridyle, tétrazolyde, trifluorométhyle, difluorométhyle, cyano, carboxyle, alkyle à chaîne droite ou ramifié, alkoxy, alkoxycarbonyle ou acyle ayant chacun jusqu'à 11 atomes de carbone dans le groupe alkyle ou avec un substituant phé-

5 nyle, qui est facultativement monosubstitué à trisubstitué avec des substituants nitro, halogéno, formyle, carbonyle ou alkoxy, acyle, alkoxy carbonyle ou alkyle à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone, qui est facultativement substitué avec un substituant hydroxyle, ou le groupe phényle est substitué avec un groupe de formule $-NR^{28}R^{29}$, $-SR^{30}$, SO_2R^{31} , $-O-SO_2R^{32}$ ou

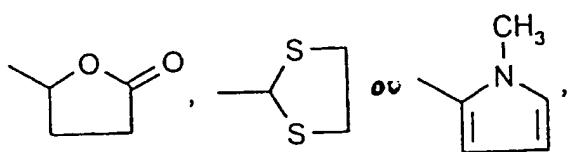
10



dans laquelle
15 R^{28} et R^{29} répondent aux définitions indiquées ci-dessus pour R^{10} et R^{11} ,
ou
 R^{28} représente l'hydrogène,
et
 R^{29} représente un groupe acyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,
20 R^{30} représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,
 R^{31} et R^{32} sont identiques ou différents et représentent un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, un groupe benzyle ou phényle, qui est facultativement substitué avec un substituant trifluorométhyle, halogéno ou alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,
25 sous réserve que A ne représente pas un groupe méthyle ou

II :
si A représente un groupe méthyle
30 R^1 , T et R^4 répondent aux définitions indiquées dans la partie I,
et, dans ce cas,
 R^2 et R^3 sont identiques ou différents et représentent l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, ou représentent un groupe formyle ou un groupe acyle, alkoxy ou alkoxy carbonyle à chaîne droite ou ramifié ayant chacun jusqu'à 8 atomes de carbone,
35 ou représentent un groupe benzoyle, qui est facultativement monosubstitué à trisubstitué avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants halogéno, cyano, carboxy, alkoxy, alkoxy carbonyle ou acyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, ou représentent un groupe de formule
 $-SO_2(NH_2)_2R^{33}$, SO_2NH_2 , $-CO-(CH_2)_dNR^{34}R^{35}$,
40 $-(CH_2)_e-CO-R^{36}$, $-CO-(CH_2)_fR^{37}$ ou $-CO-X$,
dans laquelle
 R^{33} répond à la définition mentionnée ci-dessus pour R^9 et est identique à, ou différent de, ce dernier,
 R^{34} et R^{35} sont identiques ou différents et répondent aux définitions précitées de R^{10} et R^{11} ,
45 R^{36} représente un groupe hydroxyle ou un groupe alkoxy à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,
 R^{37} répond à la définition précitée de R^{12} ou représente un groupe alkoxy ou oxyacyle à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone ou un groupe hydroxyle,
d répond à la définition précitée de a,
e représente le nombre 1, 2, 3, 4 ou 5,
f répond à la définition précitée de b,
50 g représente le nombre de 0 ou 1.
X représente un hétérocycle pentagonal saturé ou insaturé ayant jusqu'à 3 hétéroatomes du groupe comprenant N, S et/ou O, qui est facultativement monosubstitué à trisubstitué avec des substituants nitro, méthyle ou éthyle,
ou
55 X représente un résidu de formule

5



10

ou

III :

R¹, A et T répondent aux définitions indiquées dans la partie I, ou

A représente un groupe méthyle,

15 R² et R³ répondent aux définitions mentionnées ci-dessus dans la partie II,

et, dans ce cas,

20 R⁴ représente un hétérocycle penta- à heptagonal, saturé ou insaturé, qui peut contenir jusqu'à 3 atomes d'oxygène, de soufre et/ou d'azote comme hétéroatomes et auquel un noyau benzénique peut être en outre condensé, les deux noyaux étant facultativement monosubstitués à tri-substitués avec des substituants identiques ou différentes choisis dans le groupe comprenant de substituants hydroxyle, halogéno, nitro, 1H-tétrazolyde, trifluorométhyle, trifluorométhoxy, difluorométhyle, difluorométhoxy, cyano, carboxy, alkyle, alkoxy, alkoxy carbonyle ou acyle à chaîne droite ou ramifié ayant chacun jusqu'à 8 atomes de carbone, ou avec un groupe de formule -NR³⁸R³⁹, -SR⁴⁰, SO₂R⁴¹ ou -O-SO₂R⁴², dans laquelle25 R³⁸ et R³⁹ répondent aux définitions mentionnées ci-dessus pour R²⁸ et R²⁹ et sont identiques à ces derniers ou bien différents de ces derniers,R⁴⁰ répond à la définition précitée pour R³⁰,30 R⁴¹ et R⁴² sont identiques ou différents et répondent aux définitions précitées de R³¹ et R³², et leurs sels.

2. Dérivés d'amino-benzofuryle et -thiényle, répondant à la formule suivant la revendication 1, dans laquelle

I. :

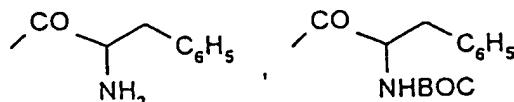
35 R¹ représente l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone ou représente le fluor, le chlore, le brome, un groupe nitro, trifluorométhyle ou un groupe de formule -OR⁵, -SR⁶ ou -NR⁷R⁸, dans laquelle40 R⁷ représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone,R⁵, R⁶ et R⁸ sont identiques ou différents et représentent l'hydrogène, un groupe cyclopropyle, cyclopentyle, cyclohexyle, quinolyde, pyridyle, imidazolyde, 1,3-thiazolyde ou thiényle, qui est facultativement substitué avec des substituants identiques ou différents choisis dans le groupe comprenant des substituants fluoro, chloro, bromo, iodo, cyano, nitro ou avec un substituant alkyle à chaîne droite ou ramifié ayant jusqu'à 5 atomes de carbone, ou

45 représentent des groupes alkyle ou alcényle à chaîne droite ou ramifiés ayant chacun jusqu'à 6 atomes de carbone, ou

représentent un groupe phényle, qui est facultativement monosubstitué à disubstitué avec des substituants identiques ou différents choisis dans le groupe comprenant des substituants nitro, fluoro, chloro, bromo, iodo, carboxy ou alkoxy carbonyle à chaîne droite ou ramifié ayant jusqu'à 5 atomes de carbone, ou

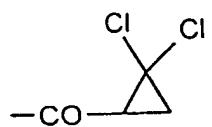
50 R⁵ représente un groupe benzyle, acétyle ou tétrahydropyrannyle,R² représente un groupe formyle ou un groupe acyle, alkoxy ou alkoxy carbonyle à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone dans le groupe alkyle,

ou représente un groupe benzoyle, qui est facultativement monosubstitué avec des substituants choisis dans le groupe comprenant des substituants fluoro, chloro, bromo, cyano, carboxy, alkoxy, alkoxy carbonyle ou acyle, à chaîne droite ou ramifié, ayant chacun jusqu'à 4 atomes de carbone dans le groupe alkyle, ou représente un groupe de formule



-SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO-(CH₂)_b-R¹², -CO-S-R¹³ ou un résidu de formule

10



15

dans lequel

R⁹ représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone, qui est facultativement substitué avec un substituant phényle, ou

représente un groupe phényle, qui est facultativement substitué avec un substituant trifluorométhyle, cyano, nitro ou alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone,

R¹⁰ et R¹¹ sont identiques ou différents et représentent l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone ou un groupe phényle,

R¹² représente un groupe alkoxy carbonyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone ou un groupe carboxy,

a représente le nombre 0, 1, 2 ou 3,

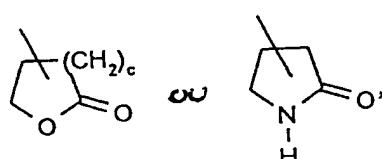
b représente le nombre 1, 2 ou 3,

R¹³ représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone,

R³ représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone, ou répond à la définition précitée de R²,

T représente un atome d'oxygène,

A représente l'hydrogène, un groupe hydroxyle, cyclopropyle, cyclobutyle, cyclopentyle, carboxyle ou un groupe alkoxy carbonyle ou alkoxy à chaîne droite ou ramifié ayant chacun jusqu'à 4 atomes de carbone, ou un groupe alkyle ou alcényle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone, chacun étant facultativement monosubstitué avec un substituant cyano, tétrazolyte, oxazolyte, oxazolynyle, thiazolyte ou un groupe de formule



45

dans laquelle

c représente le nombre 1 ou 2,

tous les noyaux étant facultativement mono-substitués avec un substituant hydroxy, fluoro, bromo, chloro ou avec un substituant alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone, ou les groupes alkyle ou alcényle sont facultativement monosubstitués avec un groupe de formule -CO-R¹⁴, -CO-NR¹⁵R¹⁶ ou -OR²¹,

dans laquelle

R¹⁴ représente un groupe hydroxyle, cyclopropoxy, cyclopentyloxy, cyclohexyloxy ou un groupe alkyle ou alkoxy à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone,

R¹⁵ et R¹⁶ sont identiques ou différents et représentent l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone, phényle ou benzyle,

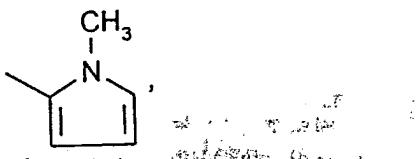
ou
 R¹⁵ représente l'hydrogène,
 et
 R¹⁶ représente un groupe hydroxyle,

5 ou
 R¹⁵ et R¹⁶ conjointement avec l'atome d'azote, forment un noyau pyrrolidinylo, morpholinyle ou pipéridinylo,

R²¹ représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,
 et

10 R⁴ représente un groupe phényle, qui est facultativement monosubstitué à trisubstitué avec des substituants identiques ou différents choisis dans le groupe comprenant des substituants hydroxyle, adamantyle, phenoxy, cyclopropyle, cyclopentyle, cyclohexyle, fluoro, chloro, bromo, iodo, nitro, tétrazolylo, furannyle, thiényle, pyridyle, trifluorométhyle, difluorométhyle, cyano, carboxy, alkyle, alkoxy, alkoxy carbonyle ou acyle à chaîne droite ou ramifié ayant chacun jusqu'à 10 atomes de carbone dans le groupe alkyle, ou
 avec un substituant phényle, qui est facultativement monosubstitué à trisubstitué avec des substituants fluoro, chloro, bromo, nitro, formyle ou alkoxy, acyle, éthoxycarbonyle ou alkyle à chaîne droite ou ramifié ayant chacun jusqu'à 4 atomes de carbone, qui est facultativement substitué avec un substituant hydroxyle, ou

20 le groupe phényle est substitué avec un groupe de formule -NR²⁸R²⁹, -SR³⁰, -SO₂R³¹, -O-SO₂R³² ou



25 30 dans laquelle
 R²⁸ et R²⁹ répondent aux définitions mentionnées ci-dessus pour R¹⁰ et R¹¹,
 ou

35 R²⁸ représente l'hydrogène,
 et
 R²⁹ représente un groupe acyle à chaîne droite ou ramifié ayant jusqu'à 6 atomes de carbone,
 R³⁰ représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone,
 R³¹ et R³² sont identiques ou différents et représentent un groupe alkyle à chaîne droite ou ramifié
 40 ayant jusqu'à 5 atomes de carbone ou un groupe phényle, qui est facultativement substitué avec un substituant trifluorométhyle, fluoro, chloro, bromo ou alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone,
 sous réserve que A ne représente pas un groupe méthyle ou

II :

45 si A représente un groupe méthyle
 R¹, T et R⁴ répondent aux définitions mentionnées dans la partie I,
 et, dans ce cas,
 R² et R³ sont identiques ou différents et représentent l'hydrogène ou des groupes alkyle à chaîne droite ou ramifiés ayant jusqu'à 4 atomes de carbone, ou
 50 représentent un groupe formyle ou un groupe acyle ou alkoxy carbonyle à chaîne droite ou ramifié ayant chaque jusqu'à 4 atomes de carbone,
 ou représentent un groupe benzoyle, qui est facultativement substitué avec des substituants choisis dans le groupe comprenant des substituants fluoro, chloro, bromo, cyano, carboxy, alkoxy, alkoxy carbonyle ou acyle à chaîne droite ou ramifié ayant chacun jusqu'à 4 atomes de carbone,
 55 ou représentent un groupe de formule
 -SO₂(NH)₉-R³³, SO₂NH₂, -CO-(CH₂)_dNR³⁴R³⁵,
 -(CH₂)_e-CO-R³⁶, -CO-(CH₂)_f-R³⁷ ou -CO-X,
 dans laquelle

R³³ répond à la définition précitée de R⁹ et est identique à, ou différent de, ce dernier,
 R³⁴ et R³⁵ sont identiques ou différents et représentent l'hydrogène ou un groupe méthyle,
 R³⁶ représente un groupe hydroxyle ou un groupe alkoxy à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone, ou bien un groupe carboxy.

5 R³⁷ répond à la définition précitée de R¹² ou représente un groupe hydroxyle ou un groupe alkoxy ou oxacyle à chaîne droite ou ramifié ayant chacun jusqu'à 4 atomes de carbone,

d répond à la définition précitée de g,

e représente le nombre 1, 2, 3 ou 4,

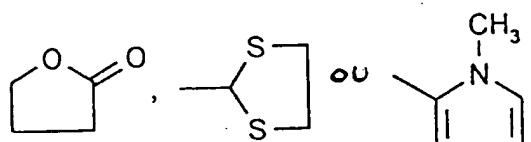
f répond à la définition précitée de g,

10 g représente le nombre de 0 ou 1,

X représente un groupe pyrrolyle, furyle ou

isoxazolyle, qui est facultativement mono-substitué à trisubstitué avec des substituants nitro, méthyle ou éthyle ou X représente un résidu de formule

15



20

ou

25 III :

R¹, A et T répondent aux définitions indiquées dans la partie I,

ou

A représente un groupe méthyle,

R² et R³ répondent aux définitions mentionnées dans la partie II,

et dans ce cas,

30 R⁴ représente un groupe pyridyle, imidazolyle, pyrazolyle, thiényle, isothiazolyle, 1,3-thiazolyle ou benzo[b]thiophényle, dans lequel tous les noyaux sont facultativement monosubstitués à trisubstitués avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants hydroxy, fluoro, chloro, bromo, iodo, nitro, 1H-tétrazolyle, trifluorométhyle, trifluorométhoxy, difluorométhyle, difluorométhoxy, cyano, carboxy, alkyle, alkoxy, alkoxy carbonyle ou acyle à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone, ou avec un groupe de formule -NR³⁸R³⁹, -SR⁴⁰, -SO₂R⁴¹ ou -O-SO₂R⁴²,

dans laquelle

35 R³⁸ et R³⁹ répondent aux définitions mentionnées ci-dessus pour R²⁸ et R²⁹ et sont identiques à ces derniers ou bien différents de ces derniers,

40 R⁴⁰ répond à la définition précitée de R³⁰,

R⁴¹ et R⁴² sont identiques ou différents et répondent aux définitions précitées de R³¹ et R³²,

et leurs sels.

3. Dérivés d'amino-benzofuryle et -thiényle, de la formule I suivant la revendication 1, dans laquelle

45

I. :

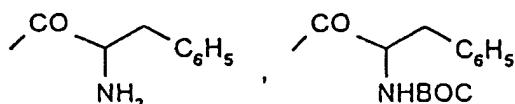
50 R¹ représente l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone, fluor, chlore, bromo, nitro, trifluorométhyle,

R² représente un groupe formyle ou un groupe acyle ou alkoxy carbonyle à chaîne droite ou ramifié ayant jusqu'à 5 atomes de carbone dans le groupe alkyle,

ou représente un groupe benzoyle, qui est facultativement substitué avec des substituants faisant partie du groupe comprenant des substituants fluoro, chloro, bromo, cyano, carboxy, alkoxy, alkoxy carbonyle ou acyle à chaîne droite ou ramifié, chacun ayant jusqu'à 3 atomes de carbone dans le groupe alkyle,

55 ou représente un groupe de formule

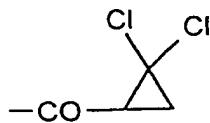
5



-SO₂R⁹, -CO-(CH₂)_aNR¹⁰R¹¹, -CO(CH₂)_b-R¹², -CO-S-R¹³
ou un résidu de formule

10

15



20

dans lequel

R⁹ représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 4 atomes de carbone, qui est facultativement substitué avec un substituant phényle, ou représente un groupe phényle, qui est facultativement substitué avec un substituant trifluorométhyle, cyano ou alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone,

25

R¹⁰ et R¹¹ sont identiques ou différents et représentent l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone ou bien un groupe phényle,

R¹² représente un groupe alkoxy carbonyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone ou un groupe carboxy,

30

a représente le nombre 0, 1, 2 ou 3,

b représente le nombre 1, 2 ou 3,

R¹³ représente un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone,

R³ représente l'hydrogène ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone, ou bien répond à la définition précitée de R²,

35

T représente un atome d'oxygène ou de soufre,

A représente l'hydrogène, un groupe hydroxyle, cyclopropyle, cyclobutyle, cyclopentyle, carboxyle ou un groupe alkoxy carbonyle ou alkoxy à chaîne droite ou ramifié ayant chacun jusqu'à 3 atomes de carbone, ou un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 5 atomes de carbone qui est facultativement monosubstitué avec un substituant cyano ou avec un groupe de formule -CO-R¹⁴, -CO-NR¹⁵R¹⁶,

40

dans laquelle

R¹⁴ représente un groupe hydroxyle, cyclopropoxy, cyclopentyloxy, cyclohexyloxy ou un groupe alkyle ou alkoxy à chaîne droite ou ramifié ayant jusqu'à 5 atomes de carbone,

45

R¹⁵ et R¹⁶ sont identiques ou différents et représentent l'hydrogène, un groupe alkyle à chaîne droite ou ramifié ayant jusqu'à 3 atomes de carbone ou un groupe phényle,

et

R⁴ représente un groupe phényle, qui est facultativement monosubstitué à trisubstitué avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants hydroxyle, adamantyle, phénoxy, N-méthylpyrrolyle, cyclopropyle, cyclopentyle, cyclohexyle, fluoro, chloro, bromo, furannyle, thiényle, pyridyle, nitro, trifluorométhyle, difluorométhyle, cyano, carboxyle, méthylthio, alkyle, alkoxy, acyle ou alkoxy carbonyle à chaîne droite ou ramifié ayant chacun jusqu'à 6 atomes de carbone, ou

50

avec un substituant phényle, qui est facultativement monosubstitué à trisubstitué avec des substituants fluoro, chloro, bromo, nitro, formyle ou alkoxy, alkoxy carbonyle, acyle ou alkyle à chaîne droite ou ramifié ayant chacun jusqu'à 4 atomes de carbone, qui est facultativement substitué avec un substituant hydroxyle,

55

sous réserve que A ne représente pas un groupe méthyle, ou

II. :

si A représente un groupe méthyle

R¹, T et R⁴ répondent aux définitions mentionnées dans la partie I,
et, dans ce cas,5 R² et R³ sont identiques ou différents et représentent l'hydrogène ou un groupe alkyle à chaîne droite ou ramifiée ayant jusqu'à 3 atomes de carbone, ou représentent un groupe formyle ou un groupe acyle ou alkoxycarbonyle à chaîne droite ou ramifiée ayant chacun jusqu'à 4 atomes de carbone,

ou représentent un groupe benzoyle, qui est facultativement substitué avec des substituants faisant partie du groupe comprenant des substituants fluoro, chloro, bromo, cyano, alkoxy ou alkoxycarbonyle à chaîne droite ou ramifiée ayant chacun jusqu'à 3 atomes de carbone,

10 ou représentent un groupe de formule -CO-NH₂, -SO₂(NH)₉R³⁷, -SO₂NH₂, -(CH₂)₆-CO-R³⁶, -CO-(CH₂)₇-R³⁷
ou -CO-X,

dans laquelle

R³³ répond à la définition précitée de R⁹ et est identique à, ou différent de, ce dernier,15 R³⁴ et R³⁵ sont identiques ou différents et représentent l'hydrogène ou un groupe méthyle, R³⁷ répond à la définition précitée de R¹² ou représente un groupe hydroxyle ou un groupe alkoxy ou oxacyle à chaîne droite ou ramifiée ayant chacun jusqu'à 4 atomes de carbone,
R³⁶ représente un groupe hydroxyle ou un groupe alkoxy à chaîne droite ou ramifiée ayant jusqu'à 3 atomes de carbone,

20 d répond à la définition précitée de a.

e représente le nombre 1, 2, 3, ou 4,

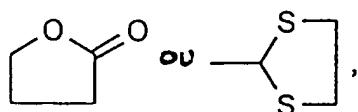
f répond à la définition précitée de b,

g représente le nombre de 0 ou 1,

X représente un groupe pyrrolyle, n-méthylpyrrolyle, furyle ou isoxazolyle, qui est facultativement monosubstitué à trisubstitué avec des substituants nitro, méthyle ou éthyle,

25 ou

X représente un résidu de formule



35

b représente le nombre 1 ou 2,

ou

III :

R¹, A et T répondent aux définitions indiquées dans la partie I,

40 ou

A représente un groupe méthyle,

R² et R³ répondent aux définitions mentionnées dans la partie II,

et, dans ce cas,

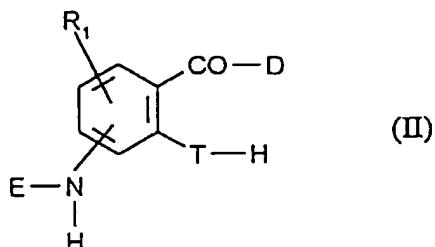
45 R⁴ représente un groupe pyridyle, qui est facultativement monosubstitué à trisubstitué avec des substituants identiques ou différents faisant partie du groupe comprenant des substituants hydroxyle, fluoro, chloro, bromo, nitro, trifluorométhyle, trifluorométhoxy, difluorométhyle, difluorométhoxy, cyano, carboxy, alkyle, alkoxy, alkoxycarbonyle ou acyle à chaîne droite ou ramifié ayant chacun jusqu'à 5 atomes de carbone,
et leurs sels.

50 4. Dérivés d'amino-benzofuryle et -thiényle suivant les revendications 1 à 3, destinés à être utilisés en thérapeutique.

5. Procédé pour la préparation de dérivés d'amino-benzofuryle et -thiényle suivant les revendications 1 à 3, caractérisé en ce que

55 [A] des composés de formule générale (II)

5



10

dans laquelle

 R^1 et T répondent aux définitions précitées,

et

 E représente un groupe acyle à chaîne droite ou ramifiée ayant jusqu'à 4 atomes de carbone, de préférence un groupe acétyle,

et

 D représente un groupe $-(CH_2)_2-(alkoxy \text{ en } C_1 \text{ à } C_4)carbonyle$,
par réaction avec des composés de formule (III)

(II)

15

20

(III)

dans laquelle

25

 R^4 répond à la définition précitée,

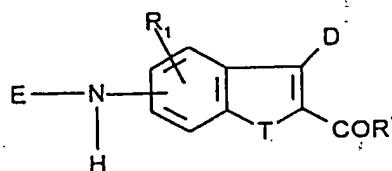
et

 L représente un groupe partant tel qu'un groupe chloro, bromo, tosylate ou mésylate,
dans des solvants inertes en présence d'une base, sont tout d'abord transformés en composés de formule
générale (Ia)

30

35

(Ia)



40

dans laquelle

 R^1 , T , D et E répondent aux définitions précitées, puis les composés (Ia)
sont amenés à réagir avec des composés de formule (IV) ou (IVa)R²-L'

(IV)

R³-L'

(IVc)

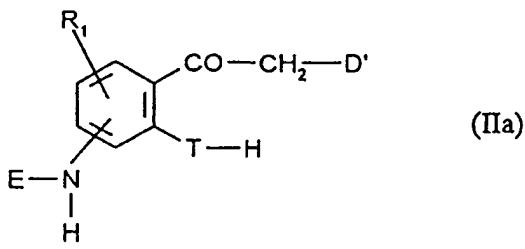
50

dans laquelle

 R^2 et R^3 répondent aux définitions précitées,

et

L' répond à la définition précitée de L et est identique à, ou différent de, ce dernier,
dans des solvants inertes, si cela est approprié, en présence d'une base,
et, dans le cas d'autres radicaux mentionnés pour la définition du substituant A, D est modifié, si cela est
approprié, par scission des groupes protecteurs, alkylation et/ou hydrolyse, ou
[B] dans le cas de A = CH_2-CO-R^{14}
tout d'abord des composés de formule générale (IIa)

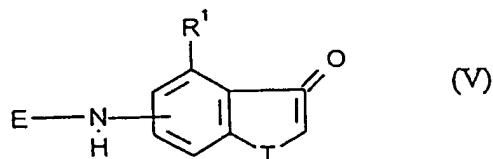


dans laquelle

E, T et R¹ répondent aux définitions précitées,

et

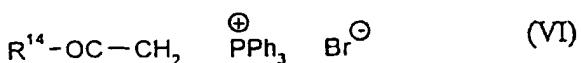
D' représente un halogène, de préférence le chlore, sont transformés en présence de NaAc et d'un alcool, de préférence l'éthanol, en composés de formule générale (V)



dans laquelle

R¹, E et T répondent aux définitions précitées,

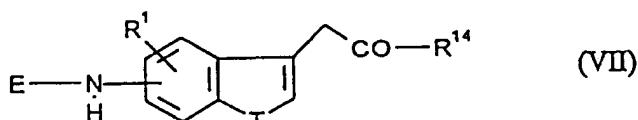
puis sont amenés à réagir avec des composés de formule générale (VI)



dans laquelle

R¹⁴ répond à la définition précitée,

ce qui donne des composés de formule générale (VII)



dans laquelle

E, R¹, T et R¹⁴ répondent aux définitions précitées, dans des solvants inertes,

et, dans une dernière étape, ces composés sont amenés à réagir avec des composés de formule générale (VIII)



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dans laquelle

R⁴ et L' répondent aux définitions précitées,

en présence de SnCl₄,

et

facultativement, les composés obtenus sont amenés à réagir avec des composés de formule générale (IV) ou (IVa).

6. Composition consistant en au moins un des dérivés d' amino-benzofuryle et -thiényle suivant les revendications 1
5 à 3 et un diluant pharmacologiquement acceptable.

7. Composition suivant la revendication 6, destinée au traitement de processus inflammatoires aigus et chroniques.

8. Procédé pour la préparation de compositions suivant les revendications 6 et 7, caractérisé en ce que le dérivé
10 d' amino-benzofuryle ou -thiényle et le diluant pharmacologiquement acceptable soient incorporés à une formulation apte à l'administration.

9. Utilisation de dérivés d' amino-benzofuryle et -thiényle suivant les revendications 1 à 3, pour la préparation de médicaments.
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10. Utilisation suivant la revendication 9, pour la préparation de médicaments destinés au traitement de processus
inflammatoires aigus et chroniques.
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